Logon 03 April 03 18:42:14
File 155:MEDLINE(R) 1966-2003/Mar W5 (c) format only 2003 The Dialog Corp.

Set	Items	Description
S9	59976	HIV/TI
S10	13052	PROTEASE/TI
S11	221900	INHIBIT?/TI
S12	4284	PROTEASE/TI(W)INHIBIT?/TI
S13	72419	INSULIN/TI
S14	91466	RESIST?/TI
S15	4838	INSULIN/TI(W)RESIST?/TI
S16	8	HIV/TI AND (PROTEASE()INHIBIT?)/TI AND (INSULIN()RESIST?)/-TI
S18	4336	(INSULIN()RESISTANCE)/TI
S19	1741	(ANTI()HIV()AGENTS()ADVERSE()EFFECTS?)/DE
S20	8	S18 AND S19
S21	971	(HIV()PROTEASE()INHIBITORS()ADVERSE()EFFECTS?)/DE
S22	15	S18 AND S21
S23	11	S22 NOT S16
S24	11225	(INSULIN()RESISTANCE)/DE
S25	48	S21 AND S24
S26	44	S25 NOT S16
S27	33	S26 NOT S23
S28	5	S20 NOT S16
S29	5	S28 NOT S27

16/9/1
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14532874 22365364 PMID: 12478066
Agent and cell-type specificity in the induction of insulin resistance by HIV protease inhibitors .
Ben-Romano Ronit; Rudich Assaf; Torok Dora; Vanounou Sharon; Riesenberg Klaris; Schlaeffer Francisc; Klip Amira; Bashan Nava
Department of Clinical Biochemistry, Ben-Gurion University of the Negev, Beer-Sheva, Israel.
AIDS (London, England) (England) Jan 3 2003, 17 (1) p23-32, ISSN 0269-9370 Journal Code: 8710219
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
OBJECTIVE: To test agent and cell-type specificity in insulin resistance induced by prolonged exposure to HIV protease inhibitors (HPI), and to assess its relation to the direct, short-term inhibition of insulin-stimulated glucose uptake. METHODS: Following prolonged (18 h) and short (5-10 min) exposure to HPI, insulin-stimulated glucose transport, protein kinase B (PKB) phosphorylation, and GLUT4 translocation were evaluated in 3T3-L1 adipocytes, fibroblasts, L6 myotubes, and L6 cells overexpressing a myc tag on the first exofacial loop of GLUT4 or GLUT1. RESULTS: Prolonged exposure of 3T3-L1 adipocytes to nelfinavir, but not to indinavir or saquinavir, resulted in increased basal lipolysis but decreased insulin-stimulated glucose transport and PKB phosphorylation. In addition, impaired insulin-stimulated glucose uptake and PKB phosphorylation were also observed in the skeletal muscle cell line L6, and in 3T3-L1 fibroblasts. Interestingly, this coincided with increased basal glucose uptake as well as with elevated total-membrane glucose transporter GLUT1 protein content. In contrast to these unique effects of nelfinavir, the mere presence of any of the agents in the 5 min transport assay inhibited insulin-stimulated glucose-uptake activity. This appeared to be caused by direct and specific interaction of the drugs with GLUT4 fully assembled at the plasma membrane, since insulin-stimulated cell-surface exposure of an exofacial myc epitope on GLUT4 was normal. CONCLUSIONS: Independent mechanisms for HPI-induced insulin resistance exist: prolonged exposure to nelfinavir interferes with insulin signaling and alters cellular metabolism of adipocytes and muscle cells, whereas a direct inhibitory effect on insulin-stimulated glucose uptake may occurs through specific interaction of HPI with GLUT4.
Tags: Human; Support, Non-U.S. Gov't
Descriptors: *HIV Protease Inhibitors--pharmacology--PD; *Insulin Resistance; Adipocytes--drug effects--DE; Adipocytes--metabolism--ME; Cell Line; Deoxyglucose--metabolism--ME; Drug Administration Schedule; Fibroblasts--drug effects--DE; Fibroblasts--metabolism--ME; Indinavir --pharmacology--PD; Lipolysis--drug effects--DE; Monosaccharide Transport Proteins--metabolism--ME; Muscle, Skeletal--drug effects--DE; Muscle, Skeletal--metabolism--ME; Nelfinavir--pharmacology--PD; Phosphorylation; Proto-Oncogene Proteins--metabolism--ME; Saquinavir--pharmacology--PD
CAS Registry No.: 0 (GLUT-1 protein); 0 (HIV Protease Inhibitors); 0 (Monosaccharide Transport Proteins); 0 (Proto-Oncogene Proteins); 0 (proto-oncogene protein akt); 127779-20-8 (Saquinavir); 150378-17-9 (Indinavir); 154-17-6 (Deoxyglucose); 159989-64-7 (Nelfinavir)
Record Date Created: 20021212
Record Date Completed: 20030306

16/9/2
DIALOG(R)File 155:MEDLINE(R)
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11904571 99347612 PMID: 10421244
Insulin resistance in HIV protease inhibitor -associated diabetes.
Yarasheski K E; Tebas P; Sigmund C; Dagogo-Jack S; Bohrer A; Turk J; Halban P A; Cryer P E; Powderly W G
Division of Endocrinology, Diabetes, and Metabolism, Washington University Medical School, St. Louis, Missouri 63110, USA. key@imgate.wustl.edu
Journal of acquired immune deficiency syndromes (1999) (UNITED STATES) Jul 1 1999, 21 (3) p209-16, ISSN 1525-4135 Journal Code: 100892005
Contract/Grant No.: AI25903; AI; NIAID; DK49393; DK; NIDDK; RR00036; RR; NCRR; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
BACKGROUND: Fasting hyperglycemia has been associated with HIV protease inhibitor (PI) therapy. OBJECTIVE: To determine whether absolute insulin deficiency or insulin resistance with relative insulin deficiency and an elevated body mass index (BMI) contribute to HIV PI-associated diabetes. DESIGN: Cross-sectional evaluation. PATIENTS: 8 healthy seronegative men, 10 nondiabetic HIV-positive patients naive to PI, 15 nondiabetic HIV-positive patients receiving PI (BMI = 26 kg/m2), 6 nondiabetic HIV-positive patients receiving PI (BMI = 31 kg/m2), and 8 HIV-positive patients with diabetes receiving PI (BMI = 34 kg/m2). All patients on PI received indinavir. MEASUREMENTS: Fasting concentrations of glucoregulatory hormones. Direct effects of indinavir (20 microM) on rat pancreatic beta-cell function in vitro. RESULTS: In hyperglycemic HIV-positive subjects, circulating concentrations of insulin, C-peptide, proinsulin, glucagon, and the proinsulin/insulin ratio were increased when compared with those of the other 4 groups ($p < .05$). Morning fasting serum cortisol concentrations were not different among the 5 groups. Glutamic acid decarboxylase (GAD) antibody titers were uncommon in all groups. High BMI was not always associated with diabetes. In vitro, indinavir did not inhibit proinsulin to insulin conversion or impair glucose-induced secretion of insulin and C-peptide from rat beta-cells. CONCLUSIONS: The pathogenesis of HIV PI-associated diabetes involves peripheral insulin resistance with insulin deficiency relative to hyperglucagonemia and a high BMI. Pancreatic beta-cell function was not impaired by indinavir. HIV PI-associated diabetes mirrors that of non-insulin-dependent diabetes mellitus and impaired insulin action in the periphery.
Tags: Animal; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Descriptors: *Anti-HIV Agents--adverse effects--AE; *Diabetes Mellitus, Insulin-Dependent--complications--CO; *HIV Infections--complications--CO; *HIV Protease Inhibitors--adverse effects--AE; *Indinavir--adverse effects--AE; *Insulin Resistance; Adult; Anti-HIV Agents--therapeutic use--TU; C-Peptide--metabolism--ME; Cells, Cultured; Cross-Sectional Studies; Glucagon--metabolism--ME; HIV Infections--drug therapy--DT; HIV Protease Inhibitors--therapeutic use--TU; Indinavir--therapeutic use--TU; Insulin--metabolism--ME; Islets of Langerhans--metabolism--ME; Phospholipases A--metabolism--ME; Proinsulin--metabolism--ME; Rats; Rats, Sprague-Dawley
CAS Registry No.: 0 (Anti-HIV Agents); 0 (C-Peptide); 0 (HIV Protease Inhibitors); 11061-68-0 (Insulin); 150378-17-9 (Indinavir); 9007-92-5 (Glucagon); 9035-68-1 (Proinsulin)
Enzyme No.: EC 3.1.1.- (Phospholipases A)
Record Date Created: 19990819
Record Date Completed: 19990819

16/9/3
DIALOG(R)File 155:MEDLINE(R)
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11597432 99030023 PMID: 9814858

Treatment with protease inhibitors associated with peripheral insulin resistance and impaired oral glucose tolerance in HIV-1-infected patients.

Walli R; Herfort O; Michl G M; Demant T; Jager H; Dieterle C; Bogner J R; Landgraf R; Goebel F D

Infektionsambulanz, Medizinische Poliklinik, Ludwig-Maximilians Universitat Munchen, Germany.

AIDS (London, England) (UNITED STATES) Oct 22 1998, 12 (15) pF167-73, ISSN 0269-9370 Journal Code: 8710219

Document type: Clinical Trial; Controlled Clinical Trial; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS; AIDS/HIV

BACKGROUND: The use of protease inhibitors in the treatment of HIV-1 infection is associated with the new onset of diabetes mellitus, hyperlipidaemia and lipodystrophy. It is unclear whether these findings are coincidental or whether they reflect a causative effect of protease inhibitors. OBJECTIVE: To evaluate the effect of treatment with protease inhibitors on insulin sensitivity, oral glucose tolerance and serum lipids in HIV-infected patients in order to determine whether treatment with protease inhibitors can cause peripheral insulin resistance. DESIGN: Cross-sectional controlled study in HIV-infected patients treated with protease inhibitors to assess insulin sensitivity, oral glucose tolerance and changes in serum lipids. METHODS: Sixty-seven patients treated with protease inhibitors, 13 therapy-naive patients and 18 HIV-negative control subjects were tested for insulin sensitivity (intravenous insulin tolerance test). In a subgroup of 24 treated patients, oral glucose tolerance was determined. Serum lipids prior to and under treatment with protease inhibitors were compared. RESULTS: Patients on protease inhibitors had a significantly decreased insulin sensitivity when compared with therapy-naive patients (median, 75 and 156 micromol/l/min, respectively; $P < 0.001$). All treated patients with impaired (n=4) or diabetic (n=9) oral glucose tolerance, and four out of 11 patients with normal glucose tolerance showed peripheral insulin resistance; all therapy-naive patients had normal insulin sensitivity. Treatment with protease inhibitors led to a significant increase in total triglycerides and cholesterol in the 67 treated patients (median increase, 113 and 37 mg/ml, respectively). CONCLUSION: Treatment with protease inhibitors is associated with peripheral insulin resistance, leading to impaired or diabetic oral glucose tolerance in some of the patients, and with hyperlipidaemia. Overall, there is a large variation in the severity and clinical presentation of protease inhibitor-associated metabolic side-effects.

Tags: Female; Human; Male

Descriptors: *Anti-HIV Agents--adverse effects--AE; *Glucose Tolerance Test; *HIV Infections--drug therapy--DT; *HIV Protease Inhibitors--adverse effects--AE; *Insulin Resistance; Adult; Cholesterol--blood--BL; HIV Infections--blood--BL; HIV Infections--physiopathology--PP; HIV-1; Middle Age; Triglycerides--blood--BL

CAS Registry No.: 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors); 0 (Triglycerides); 57-88-5 (Cholesterol)

Record Date Created: 19990107

Record Date Completed: 19990107

16/9/4
DIALOG(R)File 155:MEDLINE(R)
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11432189 98314795 PMID: 9652687

Pathogenesis of HIV -1- protease inhibitor -associated peripheral lipodystrophy, hyperlipidaemia, and insulin resistance .

Carr A; Samaras K; Chisholm D J; Cooper D A
HIV Medicine Unit, St Vincent's Hospital, Sydney, Australia. acarr@stvincents.com.au

Lancet (ENGLAND) Jun 20 1998, 351 (9119) p1881-3, ISSN 0140-6736 Journal Code: 2985213R
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS; AIDS/HIV

HIV-1 protease-inhibitor treatments are associated with a syndrome of peripheral lipodystrophy, central adiposity, breast hypertrophy in women, hyperlipidaemia, and insulin resistance. The catalytic region of HIV-1 protease, to which protease inhibitors bind, has approximately 60% homology to regions within two proteins that regulate lipid metabolism: cytoplasmic retinoic-acid binding protein type 1 (CRABP-1) and low density lipoprotein-receptor-related protein (LRP). We hypothesise that protease inhibitors inhibit CRABP-1-modified, and cytochrome P450 3A-mediated synthesis of cis-9-retinoic acid, a key activator of the retinoid X receptor; and peroxisome proliferator activated receptor type gamma (PPAR-gamma) heterodimer, an adipocyte receptor that regulates peripheral adipocyte differentiation and apoptosis. Protease-inhibitor binding to LRP would impair hepatic chylomicron uptake and triglyceride clearance by the endothelial LRP-lipoprotein lipase complex. The resulting hyperlipidaemia contributes to central fat deposition (and in the breasts in the presence of oestrogen), insulin resistance, and, in susceptible individuals, type 2 diabetes. Understanding the syndrome's pathogenesis should lead to treatment strategies and to the design of protease inhibitors that do not cause this syndrome. (25 Refs.)

Tags: Female; Human; Support, Non-U.S. Gov't
Descriptors: *HIV Protease Inhibitors--adverse effects--AE; *Hyperlipidemia--chemically induced--CI; *Insulin Resistance; *Lipodystrophy--chemically induced--CI; *Obesity--chemically induced--CI; Cytochrome P-450 Enzyme System--drug effects--DE; Diabetes Mellitus, Non-Insulin-Dependent--chemically induced--CI; HIV Protease Inhibitors --chemistry--CH; Insulin Resistance--physiology--PH; LDL-Receptor Related Protein 1; Receptors, Immunologic--drug effects--DE; Receptors, Retinoic Acid--drug effects--DE; Sequence Homology, Amino Acid
CAS Registry No.: 0 (HIV Protease Inhibitors); 0 (LDL-Receptor Related Protein 1); 0 (Receptors, Immunologic); 0 (Receptors, Retinoic Acid); 0 (retinoic acid binding protein I, cellular); 9035-51-2 (Cytochrome P-450 Enzyme System)
Record Date Created: 19980720
Record Date Completed: 19980720

16/9/5
DIALOG(R)File 155:MEDLINE(R)
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11399581 98281097 PMID: 9619798

A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance in patients receiving HIV protease inhibitors .

Carr A; Samaras K; Burton S; Law M; Freund J; Chisholm D J; Cooper D A

HIV Medicine Unit and Centre for Immunology, St Vincent's Hospital, Sydney, Australia.

AIDS (London, England) (UNITED STATES) May 7 1998, 12 (7) pF51-8, ISSN 0269-9370 Journal Code: 8710219

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS; AIDS/HIV

OBJECTIVE: To describe a syndrome of peripheral lipodystrophy (fat wasting of the face, limbs and upper trunk), hyperlipidaemia and insulin resistance in patients receiving potent HIV protease inhibitor therapy. DESIGN: Cross-sectional study. SETTING: Outpatient clinic of a university teaching hospital. PATIENTS: HIV-infected patients either receiving at least one protease inhibitor (n=116) or protease inhibitor-naive (n=32), and healthy men (n=47). INTERVENTIONS AND MAIN OUTCOME MEASURES: Lipodystrophy was assessed by physical examination and questionnaire and body composition by dual-energy X-ray absorptiometry. Fasting triglyceride, cholesterol, free fatty acid, glucose, insulin, C-peptide and fructosamine levels, other metabolic parameters, CD4 lymphocyte counts, and HIV RNA load were also assessed. RESULTS: HIV protease inhibitor-naive patients had similar body composition to healthy men. HIV protease inhibitor therapy was associated with substantially lower total body fat (13.2 versus 18.7 kg in protease inhibitor-naive patients; P=0.005), and significantly higher total cholesterol and triglyceride levels. Lipodystrophy was observed clinically in 74 (64%) protease inhibitor recipients after a mean 13.9 months and 1(3%) protease inhibitor-naive patient (P=0.0001). Fat loss occurred in all regions except the abdomen after a median 10 months. Patients with lipodystrophy experienced a relative weight loss of 0.5 kg per month and had significantly higher triglyceride, cholesterol, insulin and C-peptide levels and were more insulin-resistant than protease inhibitor recipients without lipodystrophy. Patients receiving ritonavir and saquinavir in combination had significantly lower body fat, higher lipids and shorter time to lipodystrophy than patients receiving indinavir. Three (2%) patients developed new or worsening diabetes mellitus. CONCLUSION: A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance is a common complication of HIV protease inhibitors. Diabetes mellitus is relatively uncommon.

Tags: Female; Human; Male; Support, Non-U.S. Gov't

Descriptors: *Anti-HIV Agents--adverse effects--AE; *HIV Infections --complications--CO; *HIV Infections--drug therapy--DT; *HIV Protease Inhibitors--adverse effects--AE; *Hyperlipidemia--chemically induced--CI; *Insulin Resistance; *Lipodystrophy--chemically induced--CI; Adult; Anti-HIV Agents--therapeutic use--TU; Body Composition; Cross-Sectional Studies; Diabetes Mellitus--chemically induced--CI; HIV Protease Inhibitors --therapeutic use--TU; Hyperlipidemia--complications--CO; Indinavir --adverse effects--AE; Indinavir--therapeutic use--TU; Lipodystrophy --complications--CO; Nelfinavir--adverse effects--AE; Nelfinavir --therapeutic use--TU; Risk Factors; Ritonavir--adverse effects--AE; Ritonavir--therapeutic use--TU; Saquinavir--adverse effects--AE; Saquinavir--therapeutic use--TU; Syndrome

CAS Registry No.: 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors); 0 (Ritonavir); 127779-20-8 (Saquinavir); 150378-17-9 (Indinavir); 159989-64-7 (Nelfinavir)

Record Date Created: 19980804

Record Date Completed: 19980804

16/9/6
DIALOG(R)File 155:MEDLINE(R)
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09492476 21269090 PMID: 11375344
The HIV protease inhibitor nelfinavir induces insulin resistance and increases basal lipolysis in 3T3-L1 adipocytes.
Rudich A; Vanounou S; Riesenberg K; Porat M; Tirosh A; Harman-Boehm I; Greenberg A S; Schlaeffer F; Bashan N
S. Daniel Abraham Center for Health and Nutrition, Laboratory for Multi-Disciplinary Diabetes Research, Ben-Gurion University of the Negev, Beer-Sheva, IL-84105, Israel.
Diabetes (United States) Jun 2001, 50 (6) p1425-31, ISSN 0012-1797 Journal Code: 0372763
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS
HIV protease inhibitors (HPIs) are potent antiretroviral agents clinically used in the management of HIV infection. Recently, HPI therapy has been linked to the development of a metabolic syndrome in which adipocyte insulin resistance appears to play a major role. In this study, we assessed the effect of nelfinavir on glucose uptake and lipolysis in differentiated 3T3-L1 adipocytes. An 18-h exposure to nelfinavir resulted in an impaired insulin-stimulated glucose uptake and activation of basal lipolysis. Impaired insulin stimulation of glucose up take occurred at nelfinavir concentrations >10 micromol/l (EC(50) = 20 micromol/l) and could be attributed to impaired GLUT4 translocation. Basal glycerol and free fatty acid (FFA) release were significantly enhanced with as low as 5 micromol/l nelfinavir, displaying fivefold stimulation of FFA release at 10 micromol/l. Yet, the antilipolytic action of insulin was preserved at this concentration. Potential underlying mechanisms for these metabolic effects included both impaired insulin stimulation of protein kinase B Ser 473 phosphorylation with preserved insulin receptor substrate tyrosine phosphorylation and decreased expression of the lipolysis regulator perilipin. Troglitazone pre- and cotreatment with nelfinavir partly protected the cells from the increase in basal lipolysis, but it had no effect on the impairment in insulin-stimulated glucose uptake induced by this HPI. This study demonstrates that nelfinavir induces insulin resistance and activates basal lipolysis in differentiated 3T3-L1 adipocytes, providing potential cellular mechanisms that may contribute to altered adipocyte metabolism in treated HIV patients.
Tags: Animal
Descriptors: *Adipocytes--drug effects--DE; *Adipocytes--physiology--PH; *HIV Protease Inhibitors--pharmacology--PD; *Insulin Resistance; *Lipolysis --drug effects--DE; *Nelfinavir--pharmacology--PD; 3T3 Cells; Biological Transport--drug effects--DE; Glucose--metabolism--ME; Mice; Monosaccharide Transport Proteins--metabolism--ME; Phosphorylation--drug effects--DE; Proto-Oncogene Proteins--metabolism--ME
CAS Registry No.: 0 (GLUT-4 protein); 0 (HIV Protease Inhibitors); 0 (Monosaccharide Transport Proteins); 0 (Proto-Oncogene Proteins); 0 (proto-oncogene protein akt); 159989-64-7 (Nelfinavir); 50-99-7 (Glucose)
Record Date Created: 20010525
Record Date Completed: 20010628

16/9/7
DIALOG(R)File 155:MEDLINE(R)
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09492471 21269085 PMID: 11375339

The HIV protease inhibitor indinavir impairs sterol regulatory element-binding protein-1 intranuclear localization, inhibits preadipocyte differentiation, and induces insulin resistance .

Caron M; Auclair M; Vigouroux C; Glorian M; Forest C; Capeau J

Institut National de la Sante et de la Recherche Medicale (INSERM) U 402, Faculte de Medecine Saint-Antoine, 27, rue Chaligny, 75571 Paris Cedex 12, France. caroin@st-antoine.inserm.fr

Diabetes (United States) Jun 2001, 50 (6) p1378-88, ISSN 0012-1797 Journal Code: 0372763

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

Protease inhibitors used in the treatment of HIV infection have been causally associated with lipodystrophy and insulin resistance and were shown to alter adipocyte differentiation in cultured cells. We aimed to delineate the mechanism by which indinavir impaired adipocyte function. We report that indinavir altered neither the growth nor insulin sensitivity of 3T3-F442A preadipocytes, nor did it alter the initial step of their differentiation, i.e., clonal proliferation. However, adipose conversion was inhibited by indinavir (by 50-60%), as shown by 1) the decrease in the number of newly formed adipocytes; 2) the lower level of the adipogenic protein markers, sterol regulatory element-binding protein-1 (SREBP-1), peroxisome proliferator-activated receptor-gamma (PPAR-gamma), and the insulin receptor (IR); and 3) the lack of SREBP-1 and PPAR-gamma immunoreactivity in the nucleus of most indinavir-treated cells. Partial adipose conversion also correlated with an accumulation of SREBP-1 at the nuclear periphery and an alteration in its electrophoretic mobility. Defective expression and nuclear localization of PPAR-gamma probably resulted from the decreased level of nuclear SREBP-1. Indinavir also rendered 3T3-F442A adipocytes resistant to insulin for mitogen-activated protein kinase activation at a step distal to IR substrate-1 tyrosine phosphorylation. Hence, indinavir impairs differentiation at an early step of adipose conversion probably involving the process controlling SREBP-1 intranuclear localization.

Tags: Animal; Support, Non-U.S. Gov't

Descriptors: *Adipocytes--cytology--CY; *CCAAT-Enhancer-Binding Proteins --metabolism--ME; *Cell Nucleus--metabolism--ME; *DNA-Binding Proteins --metabolism--ME; *HIV Protease Inhibitors--pharmacology--PD; *Indinavir --pharmacology--PD; *Insulin Resistance; *Stem Cells--cytology--CY; 3T3 Cells; Adipocytes--drug effects--DE; Adipocytes--physiology--PH; Cell Differentiation--drug effects--DE; Cell Division--drug effects--DE; Insulin --pharmacology--PD; Mice; Stem Cells--drug effects--DE; Stem Cells --physiology--PH; Thiazoles--pharmacology--PD; Time Factors; Tissue Distribution

CAS Registry No.: 0 (CCAAT-Enhancer-Binding Proteins); 0 (DNA-Binding Proteins); 0 (HIV Protease Inhibitors); 0 (SRE-1 binding protein); 0 (Thiazoles); 11061-68-0 (Insulin); 122320-73-4 (BRL 49653); 150378-17-9 (Indinavir)

Record Date Created: 20010525

Record Date Completed: 20010628

16/9/8
DIALOG(R)File 155:MEDLINE(R)
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08884057 20170327 PMID: 10708054
Hyperlipidemia and insulin resistance are induced by protease inhibitors independent of changes in body composition in patients with HIV infection.
Mulligan K; Grunfeld C; Tai V W; Algren H; Pang M; Chernoff D N; Lo J C; Schambelan M
Department of Medicine, University of California, San Francisco General Hospital, 94110, USA. kmulligan@sfghgcrc.ucsf.edu
Journal of acquired immune deficiency syndromes (1999) (UNITED STATES) Jan 1 2000, 23 (1) p35-43, ISSN 1525-4135 Journal Code: 100892005
Contract/Grant No.: DK45833; DK; NIDDK; DK49448; DK; NIDDK; DK54615; DK; NIDDK; +
Comment in J Acquir Immune Defic Syndr. 2001 Aug 15;27(5) 506-7; Comment in PMID 11511829
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
Although protease inhibitor (PI) therapy has improved the clinical status of patients with HIV infection, concerns have arisen that such treatment may have deleterious effects on glucose control, lipid metabolism, and body fat distribution. To determine whether initiation of PI therapy uniquely affects glucose and lipid metabolism, we analyzed paired data in HIV-infected patients before and after beginning antiretroviral therapy that included a PI (PI; N = 20) or lamivudine (3TC) but no PI (3TC; N = 9); and a control group on stable regimens that included neither of these agents (CONT: N = 12). Measurements included fasting glucose; insulin; triglycerides; total, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol; HIV RNA; CD4+ lymphocytes; weight; and total and regional body composition. Neither weight nor total or regional fat content changed significantly in any group during the period of observation. Nonetheless, in patients beginning PI therapy, there were significant increases in glucose (+9+/-3 mg/dl; p = .0136), insulin (+12.2+/-4.9 U/ml; p = .023), triglycerides (+53+/-17 mg/dl; p = .0069), and total and LDL cholesterol (+32+/-11 and +18+/-5 mg/dl; p = .0082 and .0026, respectively). None of these parameters changed significantly in the 3TC or CONT groups. The PI and 3TC groups experienced comparable increases in CD4+ lymphocytes, suggesting that the observed metabolic effects may be associated with PIs uniquely, rather than improvement in clinical status. However, it is also possible that the metabolic effects of PIs are associated with more effective viral suppression, because a greater proportion of patients in the PI group achieved undetectable levels of virus. We conclude that changes in glucose and lipid metabolism are induced by PI therapy in the absence of significant changes in weight or fat distribution. Longer periods of follow-up will be required to determine the clinical significance of these changes. However, at the moment, the risks associated with these metabolic effects do not appear to outweigh improvements in survival seen with PI therapy.
Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Descriptors: *Body Composition--drug effects--DE; *HIV Infections --metabolism--ME; *HIV Protease Inhibitors--pharmacology--PD; *Hyperlipidemia; *Insulin Resistance; Adult; Fasting; HIV Infections--drug therapy--DT; Hydrocortisone--blood--BL; Longitudinal Studies; Middle Age; Testosterone--blood--BL
CAS Registry No.: 0 (HIV Protease Inhibitors); 50-23-7 (Hydrocortisone); 57-85-2 (Testosterone)
Record Date Created: 20000316
Record Date Completed: 20000316

23/9/1
DIALOG(R)File 155:MEDLINE(R)
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14390634 22416054 PMID: 12541993
AACTG recommendations for metabolic problems. Guide covers insulin resistance and diabetes.
AIDS alert (United States) Jan 2003, 18 (1) p6, ISSN 0887-0292
Journal Code: 8608900
Document type: Newspaper Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIDS/HIV
The Adult AIDS Clinical Trials Group has responded to research showing a link between HIV antiretroviral treatment and metabolic disorders with guidelines that offer recommendations for assessing, monitoring, and treating the problem. According to the AACTG, up to 40% of HIV patients on a protease inhibitor-containing regimen will have impaired glucose tolerance caused by significant insulin resistance, which can lead to increased risk of cardiovascular complication.
Tags: Human
Descriptors: Diabetes Mellitus--chemically induced--CI; *HIV Infections --drug therapy--DT; * HIV Protease Inhibitors -- adverse effects --AE ; *Insulin Resistance; *Practice Guidelines; *Reverse Transcriptase Inhibitors--adverse effects--AE; Blood Glucose--analysis--AN; Diet; Glucose Tolerance Test; Lipids--blood--BL
CAS Registry No.: 0 (Blood Glucose); 0 (HIV Protease Inhibitors); 0 (Lipids); 0 (Reverse Transcriptase Inhibitors)
Record Date Created: 20030115
Record Date Completed: 20030130

23/9/2
DIALOG(R)File 155:MEDLINE(R)
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11983882 99428979 PMID: 10499191

Diabetes, insulin resistance and dyslipidaemia in lipodystrophic HIV-infected patients on highly active antiretroviral therapy (HAART).

Vigouroux C; Gharakhanian S; Salhi Y; Nguyen T H; Chevenne D; Capeau J; Rozenbaum W

Service de Biochimie, Hopital Rothschild, Paris, France.

Diabetes & metabolism (FRANCE) Sep 1999, 25 (3) p225-32, ISSN 1262-3636 Journal Code: 9607599

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS; AIDS/HIV

This study assessed glucose tolerance, insulin sensitivity and lipid parameters in HIV-infected patients presenting with lipodystrophy during HAART including protease inhibitors. Fourteen consecutive patients from Rothschild Hospital treated with HAART and presenting with marked facial lipoatrophy were evaluated. A 75 g oral glucose tolerance test (OGTT) with measurement of plasma glucose, insulin, proinsulin and free fatty acids at T0, 30, 60, 90 and 120 min was performed. Lipid parameters (triglycerides, cholesterol, apolipoproteins A1 and B) were studied as well as nutritional and inflammatory markers (albumin, prealbumin, transferrin, haptoglobin, orosomucoid, C-reactive protein), endocrine and cytokine parameters (thyrotropin, cortisol, leptin, interleukin-6), HIV viral load and CD4-lymphocyte count. These patients were compared with 20 non-lipodystrophic protease inhibitor-treated patients. The measurements performed during OGTT showed that among the 14 lipodystrophic patients, 11 (79%) presented with diabetes (5 patients) or normal glucose tolerance but with insulin resistance (6 patients). This frequency was strikingly different in the group of nonlipodystrophic patients, which included only 4 (20%) presenting with diabetes (1 patient), or impaired glucose tolerance (2 patients), or normal glucose tolerance but with insulin resistance (1 patient). Hypertriglyceridaemia was present in 11 lipodystrophic (79%) versus 7 nonlipodystrophic patients (35%). Nutritional and endocrine measurements were normal. An abnormal processing of proinsulin to insulin was excluded. Thus, lipodystrophy during HAART was associated with diabetes, insulin resistance and hypertriglyceridaemia. Diabetes, diagnosed by basal and/or 120 min-OGTT glycaemia, seems more frequent than previously described. The therapeutic consequences of these results deserve evaluation in clinical trials.

Tags: Female; Human; Male

Descriptors: Anti-HIV Agents--adverse effects--AE; *Diabetes Mellitus --etiology--ET; *HIV Infections--drug therapy--DT; * HIV Protease Inhibitors -- adverse effects --AE; *Hyperlipidemia--etiology--ET; *Insulin Resistance; *Lipodystrophy--chemically induced--CI; Adult; Aged; Apolipoproteins--blood--BL; Blood Glucose--metabolism--ME; Cholesterol --blood--BL; Drug Therapy, Combination; Fatty Acids, Nonesterified--blood --BL; Glucose Tolerance Test; Insulin--blood--BL; Lipodystrophy --physiopathology--PP; Middle Age; Proinsulin--blood--BL; Retrospective Studies; Triglycerides--blood--BL

CAS Registry No.: 0 (Anti-HIV Agents); 0 (Apolipoproteins); 0 (Blood Glucose); 0 (Fatty Acids, Nonesterified); 0 (HIV Protease Inhibitors); 0 (Triglycerides); 11061-68-0 (Insulin); 57-88-5 (Cholesterol); 9035-68-1 (Proinsulin)

Record Date Created: 19991018

Record Date Completed: 19991018

23/9/3
DIALOG(R)File 155:MEDLINE(R)
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11856495 99297598 PMID: 10371188
Effects of metformin on insulin resistance and central adiposity in patients receiving effective protease inhibitor therapy.
Saint-Marc T; Touraine J L
AIDS (London, England) (ENGLAND) May 28 1999, 13 (8) p1000-2, ISSN 0269-9370 Journal Code: 8710219
Document type: Clinical Trial; Letter; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
Tags: Female; Human; Male
Descriptors: Adipose Tissue--drug effects--DE; * HIV Protease Inhibitors -- adverse effects --AE; *Hypoglycemic Agents--therapeutic use--TU; *Insulin Resistance; *Metformin--therapeutic use--TU; Adult; Anti-HIV Agents--adverse effects--AE; Anti-HIV Agents--therapeutic use--TU; Body Composition; HIV Infections--drug therapy--DT; HIV Protease Inhibitors--therapeutic use--TU; Insulin--blood--BL
CAS Registry No.: 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors); 0 (Hypoglycemic Agents); 11061-68-0 (Insulin); 657-24-9 (Metformin)
Record Date Created: 19990902
Record Date Completed: 19990902

23/9/4
DIALOG(R)File 155:MEDLINE(R)
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09866823 21681329 PMID: 11823959
Acanthosis nigricans: a new manifestation of insulin resistance in patients receiving treatment with protease inhibitors.
Mellor-Pita Susana; Yebra-Bango Miguel; Alfaro-Martinez Joaquin; Suarez Emilio
Servicio de Medicina Interna 1, Clinica Puerta de Hierro Universidad Autonoma de Madrid, 28035 Madrid, Spain.
Clinical infectious diseases - an official publication of the Infectious Diseases Society of America (United States) Mar 1 2002, 34 (5) p716-7, ISSN 1537-6591 Journal Code: 9203213
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Tags: Case Report; Human; Male
Descriptors: Acanthosis Nigricans--etiology--ET; * HIV Protease Inhibitors -- adverse effects --AE; *Insulin Resistance; Adult; Diabetes Mellitus--etiology--ET; Didanosine--adverse effects--AE; HIV Infections --complications--CO; HIV Infections--drug therapy--DT; Ritonavir--adverse effects--AE; Zidovudine--adverse effects--AE
CAS Registry No.: 0 (HIV Protease Inhibitors); 0 (Ritonavir); 30516-87-1 (Zidovudine); 69655-05-6 (Didanosine)
Record Date Created: 20020201
Record Date Completed: 20020228

23/9/5
DIALOG(R)File 155:MEDLINE(R)
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09806493 21614799 PMID: 11747288
Acquired immunodeficiency syndrome-related insulin resistance and lipodystrophy: a multifactorial viral and iatrogenic condition.
Kino T; Chrousos G P
Endocrine practice - official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists (United States) Nov-Dec 2001, 7 (6) p480-4, ISSN 1530-891X
Journal Code: 9607439
Comment on Endocr Pract. 2001 Nov-Dec;7(6) 430-7; Comment on PMID 11747278
Document type: Comment; Editorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Tags: Human
Descriptors: Acquired Immunodeficiency Syndrome--drug therapy--DT; * HIV Protease Inhibitors -- adverse effects --AE; *Insulin Resistance; *Lipodystrophy--etiology--ET; Acquired Immunodeficiency Syndrome --complications--CO; Acquired Immunodeficiency Syndrome--metabolism--ME; Lipodystrophy--chemically induced--CI; Lipodystrophy--metabolism--ME; Retroviridae Proteins--adverse effects--AE; Syndrome
CAS Registry No.: 0 (HIV Protease Inhibitors); 0 (Retroviridae Proteins)
Record Date Created: 20011218
Record Date Completed: 20020213

23/9/6
DIALOG(R)File 155:MEDLINE(R)
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09806483 21614789 PMID: 11747278

Syndrome of lipodystrophy, hyperlipidemia, insulin resistance , and diabetes in treated patients with human immunodeficiency virus infection.

Graber A L

Division of Endocrinology and Diabetes, Vanderbilt University School of Medicine, Vanderbilt Medical Center, 2558 TVC, Nashville, TN 37232, USA.

Endocrine practice - official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists (United States) Nov-Dec 2001, 7 (6) p430-7, ISSN 1530-891X
Journal Code: 9607439

Comment in Endocr Pract. 2001 Nov-Dec;7(6) 480-4; Comment in PMID 11747288

Document type: Journal Article; Review; Review, Multicase

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

OBJECTIVE: To describe the syndrome of lipodystrophy, hyperlipidemia, insulin resistance, and diabetes in patients with human immunodeficiency virus (HIV) infection treated with protease inhibitor drugs. METHODS: This is a case series of patients referred from an infectious disease clinic to a diabetes-endocrinology clinic in an academic medical center because of severe metabolic problems that occurred during the course of otherwise-successful treatment of HIV infection. The clinical course, abnormalities on physical examination, laboratory data, and complications are described and analyzed. The pathogenesis of the syndrome is discussed and compared with that of type 2 diabetes, lipoatrophic diabetes, and mouse models of lipodystrophy. RESULTS: In six male patients receiving antiretroviral therapy for HIV infection, a syndrome of lipoatrophy of the face, legs, and buttocks, hyperlipidemia (predominantly hypertriglyceridemia), and type 2 diabetes mellitus was noted. Two patients had pronounced abdominal obesity, in contrast to their thin extremities. Five of the six patients were receiving protease inhibitor drugs, which have been thought to contribute to metabolic abnormalities. In two patients, ischemic heart disease had developed. CONCLUSION: Protease inhibitors frequently cause insulin resistance and lipoatrophy in subcutaneous adipose tissue. These abnormalities are associated with visceral adiposity, hyperlipidemia, diabetes, and cardiovascular consequences and represent an important and unsolved problem in the treatment of HIV-infected patients. (29 Refs.)

Tags: Case Report; Human; Male

Descriptors: Diabetes Mellitus, Non-Insulin-Dependent--complications--CO; *HIV Infections--drug therapy--DT; * HIV Protease Inhibitors -- adverse effects --AE; *Hyperlipidemia--chemically induced--CI; *Insulin Resistance; *Lipodystrophy--chemically induced--CI; Adult; HIV Infections --metabolism--ME; Hyperlipidemia--complications--CO; Lipodystrophy --complications--CO; Middle Age; Myocardial Ischemia--etiology--ET; Obesity --etiology--ET; Syndrome

CAS Registry No.: 0 (HIV Protease Inhibitors)

Record Date Created: 20011218

Record Date Completed: 20020213

23/9/7
DIALOG(R)File 155:MEDLINE(R)
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09738637 21540235 PMID: 11684928

Lipodystrophy in HIV-1-positive patients is associated with insulin resistance in multiple metabolic pathways.

van der Valk M; Bisschop P H; Romijn J A; Ackermans M T; Lange J M; Endert E; Reiss P; Sauerwein H P

National AIDS Therapy Evaluation Center and Department of Infectious Diseases, Tropical Medicine and AIDS, Academic Medical Center, Amsterdam, The Netherlands. m.vandervalk@amc.uva.nl

AIDS (London, England) (England) Nov 9 2001, 15 (16) p2093-100, ISSN 0269-9370 Journal Code: 8710219

Comment in AIDS. 2001 Nov 9;15(16) 2187-8; Comment in PMID 11684939

Document type: Clinical Trial; Journal Article; Randomized Controlled Trial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS; AIDS/HIV

BACKGROUND: Treatment for HIV-1 infection is complicated by fat redistribution (lipodystrophy). This is associated with insulin resistance concerning glucose uptake. Our aim was to characterize glucose metabolism more comprehensively in HIV-1-infected patients with lipodystrophy. We assessed glucose disposal and its pathways, glucose production, plasma free fatty acid (FFA) levels, and the degree to which these parameters could be suppressed by insulin. METHODS: Six HIV-1-infected men on protease inhibitor-based HAART with lipodystrophy (HIV+LD) were studied. The results were compared with those in six matched healthy male volunteers. Insulin sensitivity was quantified by hyperinsulinemic euglycaemic clamp. Glucose production and uptake were assessed by tracer dilution employing 6,6D(2)-glucose. RESULTS: At post-absorptive insulin concentrations, glucose production was 47% higher in HIV+LD than controls (P = 0.025). During clamp, glucose production was suppressed by 53% in HIV+LD, but by 85% in controls (P = 0.004). Glucose disposal increased in both groups, but by only 27% in HIV+LD versus 201% in controls (P = 0.004). Consequently, insulin-stimulated total glucose disposal was lower in HIV+LD patients (P = 0.006). Non-oxidative glucose disposal as percentage of total disposal did not differ significantly between groups (63% in HIV+LD and 62% in controls). Baseline plasma FFA concentrations were higher (0.60 versus 0.35 mmol/l; P = 0.024), whereas FFA decline during hyperinsulinemia was less (65 versus 85%; P = 0.01) in HIV+LD versus controls. CONCLUSIONS: Post-absorptive glucose production is increased in HIV-1-infected patients with lipodystrophy. Moreover, both the ability of insulin to suppress endogenous glucose production and lipolysis, and to stimulate peripheral glucose uptake and its metabolic pathways is reduced, indicating severe resistance concerning multiple effects of insulin.

Tags: Human; Male; Support, Non-U.S. Gov't

Descriptors: HIV Infections--drug therapy--DT; * HIV Protease Inhibitors -- adverse effects --AE; *Insulin Resistance; *Lipodystrophy --metabolism--ME; Adult; Anti-HIV Agents--therapeutic use--TU; Body Composition; Dideoxynucleosides--therapeutic use--TU; Drug Therapy, Combination; Fatty Acids--blood--BL; Glucose--metabolism--ME; HIV Protease Inhibitors--therapeutic use--TU; HIV-1--physiology--PH; Lipodystrophy --chemically induced--CI; Middle Age; Reverse Transcriptase Inhibitors --therapeutic use--TU

CAS Registry No.: 0 (Anti-HIV Agents); 0 (Dideoxynucleosides); 0 (Fatty Acids); 0 (HIV Protease Inhibitors); 0 (Reverse Transcriptase Inhibitors); 0 (abacavir); 50-99-7 (Glucose)

Record Date Created: 20011030

Record Date Completed: 20020118

23/9/8
DIALOG(R)File 155:MEDLINE(R)
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09693413 21485801 PMID: 11600834
Getting to the HAART of insulin resistance .
Nolan D; Mallal S
AIDS (London, England) (England) Oct 19 2001, 15 (15) p2037-41,
ISSN 0269-9370 Journal Code: 8710219
Comment on AIDS. 2001 Oct 19;15(15) 1993-2000; Comment on PMID 11600828
Document type: Comment; Editorial; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
(39 Refs.)
Tags: Human
Descriptors: Anti-HIV Agents--adverse effects--AE; *Antiretroviral Therapy, Highly Active--adverse effects--AE; *HIV Infections--drug therapy --DT; * HIV Protease Inhibitors -- adverse effects --AE; *Insulin Resistance; *Lipodystrophy--physiopathology--PP; Lipodystrophy--etiology --ET; Reverse Transcriptase Inhibitors--adverse effects--AE
CAS Registry No.: 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors); 0 (Reverse Transcriptase Inhibitors)
Record Date Created: 20011015
Record Date Completed: 20020103

23/9/9
DIALOG(R)File 155:MEDLINE(R)
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09567648 21349861 PMID: 11458032
Selective aspects of the insulin resistance syndrome.
Corry D B; Tuck M L
UCLA Olive View Medical Center, Sylmar, California, USA.
Current opinion in nephrology and hypertension (England) Jul 2001, 10 (4) p507-14, ISSN 1062-4821 Journal Code: 9303753
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

There is increasing recognition of new features in the insulin resistance syndrome and its association with new disease states or treatment modalities. Recent additions to the list of features in the insulin resistance syndrome include elevated non-esterified fatty acids, abnormalities in visceral fat metabolism, elevated uric acid, elevated hematocrit, endothelial dysfunction, abnormalities in glucocorticoids, and differences in the phenotypic expression of the syndrome between men and women. A critical factor that may be inherent in the syndrome is the distribution and metabolism of visceral fat. This finding is also accompanied by the recognition of the role of non-esterified fatty acids as a cause of many of the risk factors in the insulin resistance syndrome. Elevated non-esterified fatty acids contribute to hypertension, glucose intolerance and increased arteriosclerosis. Elevated cortisol levels and disrupted metabolism, as well as abnormalities in the hypothalamic-pituitary-adrenal axis are seen in the insulin resistance syndrome. In women, adipose cells express fewer glucocorticoid receptors and less of the enzyme that metabolizes cortisol, 11beta-hydroxysteroid dehydrogenase. Several inflammatory factors such as tumor necrosis factor-alpha may be an etiologic link in the risk found in the insulin resistance syndrome. Certain cases of the syndrome appear to be related to specific drug therapies (steroids, immunosuppressive agents and antiretroviral agents), as seen in transplant patients and HIV-infected individuals. (96 Refs.)

Tags: Female; Human; Male
Descriptors: *Insulin Resistance--physiology--PH; Fatty Acids, Nonesterified--physiology--PH; HIV Protease Inhibitors -- adverse effects --AE; Hormones--physiology--PH; Inflammation--physiopathology--PP; Kidney Transplantation--adverse effects--AE; Kidney Transplantation --physiology--PH; Obesity--physiopathology--PP; Sex Characteristics; Steroids--physiology--PH; Syndrome
CAS Registry No.: 0 (Fatty Acids, Nonesterified); 0 (HIV Protease Inhibitors); 0 (Hormones); 0 (Steroids)
Record Date Created: 20010717
Record Date Completed: 20011011

23/9/10
DIALOG(R)File 155:MEDLINE(R)
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09428589 21196464 PMID: 11298728
Anti-retroviral therapy, insulin resistance and lipodystrophy.
Gan S K; Samaras K; Carr A; Chisholm D
Diabetes and Metabolism Research Program, Garvan Institute of Medical Research, St Vincent's Hospital, Sydney, NSW, Australia.
Diabetes, obesity & metabolism (England) Apr 2001, 3 (2) p67-71, ISSN 1462-8902 Journal Code: 100883645
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
(38 Refs.)
Tags: Animal; Human
Descriptors: *Antiretroviral Therapy, Highly Active--adverse effects--AE; *Insulin Resistance; *Lipodystrophy--chemically induced--CI; Cardiovascular Diseases--etiology--ET; HIV Protease Inhibitors -- adverse effects --AE; Hypertriglyceridemia--chemically induced--CI; Syndrome
CAS Registry No.: 0 (HIV Protease Inhibitors)
Record Date Created: 20010412
Record Date Completed: 20010607

23/9/11
DIALOG(R)File 155:MEDLINE(R)
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08844369 20128721 PMID: 10665336

Human obesity and thinness, hyperlipidemia, hyperglycemia, and insulin resistance associated with HIV1 protease inhibitors. Prevention by alternating several antiproteases in short sequences.

Mathe G

Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie (FRANCE) Dec 1999, 53 (10) p449-51, ISSN 0753-3322 Journal Code: 8213295
Document type: Editorial; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV

In 1997, and mainly in 1998 and 1999, a lipodystrophic syndrome with central obesity, peripheral fat loss, hyperlipidemia, hyperglycemia and insulin-resistant-diabetes II, was described as the most frequent manifestation of toxicity of HIV1 virostatic therapy, associated with protease inhibitors (PI) in 83% of the patients who used them for 10 months. Almost similar syndromes had been published before the latter, due, for example, to graft vs host reaction, or autoimmunity against insulin receptors, or to caloric excess in the presence of androgens (the mediator being hyperinsulinemia). Carr and Cooper have presented an original pathophysiological mechanism for the PI-associated syndrome, residing in 63% homology between HIV1-protease and the 3-low-density-lipoprotein-receptor-related protein (LRP), and in 53% homology between this virus enzyme and retinoid-binding-protein type 1 (CRAB1). The treatment should be more subtle than those of common obesity and/or type II diabetes. This HIV1-protease inhibitor toxicity can be prevented by alternating several antiproteases in short sequences of the different ones. (34 Refs.)

Tags: Human
Descriptors: Diabetes Mellitus, Non-Insulin-Dependent--chemically induced --CI; *HIV Infections--drug therapy--DT; * HIV Protease Inhibitors -- adverse effects --AE; *Hyperglycemia--chemically induced--CI; *Hyperlipidemia--chemically induced--CI; *Insulin Resistance; *Obesity --chemically induced--CI; *Thinness--chemically induced--CI; Acquired Immunodeficiency Syndrome--drug therapy--DT; Drug Administration Schedule; HIV Protease Inhibitors--administration and dosage--AD
CAS Registry No.: 0 (HIV Protease Inhibitors)
Record Date Created: 20000225
Record Date Completed: 20000225

27/9/1
DIALOG(R)File 155:MEDLINE(R)
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14347450 22308826 PMID: 12422251
Adverse drug reactions to protease inhibitors.
Manchanda Tarang; Schiedel Dan; Fischer Dan; Dekaban Gregory A; Rieder Michael J; et al
John P Robarts Research Institute, Department of Paediatrics, University of Western Ontario, London.
Canadian journal of clinical pharmacology = Journal canadien de pharmacologie clinique (Canada) Fall 2002, 9 (3) p137-46, ISSN 1198-581X Journal Code: 9804162
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Protease inhibitors are drugs that are commonly used in the therapy of people living with HIV infection. These drugs are commonly used in combination and act by inhibiting viral protease, blocking viral replication. Adverse drug reactions to protease inhibitors include gastrointestinal problems, rash and metabolic disturbances. The metabolic derangements associated with protease inhibitor therapy are the most problematic adverse events associated with therapy, and vary in incidence from drug to drug. These derangements include hyperlipidemia, abnormal fat distribution (lipodystrophy) and impaired glucose tolerance, which is believed to be due to peripheral insulin resistance. Clinicians caring for patients being treated with protease inhibitors must be vigilant for adverse events, notably those involving altered lipid and glucose metabolism. (98 Refs.)
Tags: Human; Support, Non-U.S. Gov't
Descriptors: HIV Protease Inhibitors -- adverse effects --AE; Drug Therapy, Combination; Glucose--metabolism--ME; HIV Infections--drug therapy --DT; HIV Protease Inhibitors--metabolism--ME; HIV Protease Inhibitors --therapeutic use--TU; Hyperlipidemia--chemically induced--CI; Insulin Resistance ; Lipodystrophy--chemically induced--CI
CAS Registry No.: 0 (HIV Protease Inhibitors); 50-99-7 (Glucose)
Record Date Created: 20021107
Record Date Completed: 20030121

27/9/2
DIALOG(R)File 155:MEDLINE(R)
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14211995 22348783 PMID: 12462148
Investigating the cellular targets of HIV protease inhibitors: implications for metabolic disorders and improvements in drug therapy.
Murata H; Hruz P W; Mueckler M; et al
Department of Cell Biology and Physiology, Washington University School of Medicine, 660 South Euclid Avenue, St. Louis, MO 63110, USA.
Curr Drug Targets Infect Disord (Netherlands) Mar 2002, 2 (1) p1-8, ISSN 1568-0053 Journal Code: 101128002
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The use of HIV protease inhibitors (PIs) may be associated with serious adverse side effects that include fat tissue redistribution, hyperlipidemia, and insulin resistance. The etiology of this toxic metabolic syndrome (commonly referred to as 'HIV lipodystrophy syndrome') remains to be elucidated. The interpretation of available clinical data on this subject is complicated in part by the pervasiveness of potential confounding factors that cannot be easily eliminated or adequately controlled. Numerous investigators have examined the effects of PIs on cellular processes in model systems amenable to extensive experimental manipulations; the present review primarily focuses on these efforts. The ultimate goal is the unambiguous identification of discrete cellular targets being surreptitiously impacted by PIs. SREBP and Glut4 are discussed as candidate target molecules in this context. The identification of cellular factors interacting with PIs represents a necessary first step in devising rational strategies for improvement in drug therapy. (49 Refs.)
Tags: Animal; Human
Descriptors: HIV Infections--complications--CO; * HIV Protease Inhibitors -- adverse effects --AE; *Metabolic Diseases--chemically induced--CI; Adipocytes--drug effects--DE; Adipose Tissue--drug effects--DE ; HIV Infections--drug therapy--DT; HIV Protease Inhibitors--pharmacology --PD; HIV Protease Inhibitors--therapeutic use--TU; Hyperlipidemia--blood --BL; Hyperlipidemia--chemically induced--CI; Insulin Resistance --physiology--PH; Metabolic Diseases--pathology--PA
CAS Registry No.: 0 (HIV Protease Inhibitors)
Record Date Created: 20021203
Record Date Completed: 20021224

27/9/3
DIALOG(R)File 155:MEDLINE(R)
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14015908 22296691 PMID: 12410482
Switching effective antiretroviral therapy: a review.
Drechsler Henning; Powderly William G; et al
Division of Infectious Diseases, Washington University School of Medicine, St. Louis, Missouri 63110, USA.
Clinical infectious diseases - an official publication of the Infectious Diseases Society of America (United States) Nov 15 2002, 35 (10) p1219-30, ISSN 1537-6591 Journal Code: 9203213
Contract/Grant No.: AI-25903; AI; NIAID; DK-59532; DK; NIDDK; +
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
One approach to target the long-term metabolic toxicity and disfiguring body-shape changes associated with antiretroviral therapy is to switch one component of a regimen to an alternative drug, usually from a different class of antiretrovirals. Most commonly, substitutions have involved protease inhibitors, but the thymidine analogue nucleosides, especially stavudine, have been investigated more recently. Certain trends from these studies have emerged. First, if the patient has had sustained viral suppression, switching therapy is generally virologically safe. Second, metabolic disturbances, such as insulin resistance and dyslipidemia, appear to be at least partially reversible. Substitution of other agents for protease inhibitors has not been associated with reversal or improvement in fat redistribution. Studies in which thymidine analogue reverse-transcriptase inhibitors have been switched have reported modest improvements in peripheral lipoatrophy. Larger, controlled, long-term studies and a more standardized approach to definition of metabolic and morphological abnormalities are needed. (57 Refs.)
Tags: Human; Support, U.S. Gov't, P.H.S.
Descriptors: *Anti-HIV Agents--therapeutic use--TU; *HIV Infections--drug therapy--DT; *HIV Protease Inhibitors--therapeutic use--TU; *Hyperlipidemia --etiology--ET; Anti-HIV Agents--adverse effects--AE; Antiretroviral Therapy, Highly Active; HIV Protease Inhibitors -- adverse effects --AE; Insulin Resistance ; Patient Compliance; Quality of Life; Treatment Outcome
CAS Registry No.: 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors)
Record Date Created: 20021031
Record Date Completed: 20021118

27/9/4
DIALOG(R)File 155:MEDLINE(R)
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11727903 99164654 PMID: 10065260
[Lipodystrophy and 'buffalo hump' during treatment with HIV protease inhibitors]
Lipodystrofie en 'buffalo hump' bij de behandeling met HIV-proteaseremmers.
Dieleman J P; Hillebrand-Haverkort M E; van der Ende M E; Sturkenboom M C ; Lange J M; Stricker B H
Sectie Farmaco-epidemiologie van de afdelingen Epidemiologie en Biostatistiek en Inwendige Geneeskunde, Erasmus Medisch Centrum, Rotterdam.
Nederlands tijdschrift voor geneeskunde (NETHERLANDS) Dec 26 1998, 142 (52) p2856-60, ISSN 0028-2162 Journal Code: 0400770
Document type: Journal Article ; English Abstract
Languages: DUTCH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
In three patients, a 36-year-old HIV seropositive homosexual man and two women aged 35 and 59 years who had acquired HIV infection through heterosexual contact, signs of lipodystrophy developed after prolonged anti-HIV triple therapy. The observed syndrome is seen after prolonged use of HIV protease inhibitors: it is characterized by peripheral fat wasting, central fat accumulation, hyperlipidaemia and insulin resistance. Typically the subcutaneous fatty tissue disappears resulting in prominent zygomata, veins and muscles and thinning of extremities and buttocks. In addition to abdominal fat accumulation, there have been reports on the occurrence of a dorsocervical fat pad, the so-called buffalo hump. Lipodystrophy caused by protease inhibitors is a risk factor for cardiovascular disease. Recognition of the syndrome is essential for adequate follow-up and possible treatment.
Tags: Case Report; Female; Human; Male
Descriptors: HIV Infections--drug therapy--DT; * HIV Protease Inhibitors -- adverse effects --AE; *Lipodystrophy--etiology--ET; Adult; CD4 Lymphocyte Count; Cardiovascular Diseases--etiology--ET; Diabetes Mellitus, Non-Insulin-Dependent--etiology--ET; Drug Therapy, Combination; HIV Infections--complications--CO; HIV Protease Inhibitors--administration and dosage--AD; Hyperlipidemia--etiology--ET; Indinavir--administration and dosage--AD; Indinavir--adverse effects--AE; Insulin Resistance --physiology--PH; Middle Age; Nevirapine--administration and dosage--AD; Reverse Transcriptase Inhibitors--administration and dosage--AD; Treatment Outcome; Wasting Syndrome--etiology--ET
CAS Registry No.: 0 (HIV Protease Inhibitors); 0 (Reverse Transcriptase Inhibitors); 129618-40-2 (Nevirapine); 150378-17-9 (Indinavir)
Record Date Created: 19990413
Record Date Completed: 19990413

27/9/5
DIALOG(R)File 155:MEDLINE(R)
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10151993 22145220 PMID: 12149814
[Changes in carbohydrate metabolism in the HIV/AIDS patient]
Alteraciones del metabolismo hidrocarbonado en el paciente VIH/SIDA.
Gomez Candela C; de Cos Blanco A I; Mateo R; Castro E; Lorenzo A; Polo R
Unidad de Nutricion Clinica y Dietetica, Hospital Universitario La Paz, Paseo de la Castellana, 261, 28046 Madrid. nutricion@hulp.insalud.es
Nutricion hospitalaria - organo oficial de la Sociedad Espanola de Nutricion Parenteral y Enteral (Spain) May-Jun 2002, 17 (3) p147-53, ISSN 0212-1611 Journal Code: 9100365
Document type: Journal Article; Review; Review, Tutorial ; English Abstract
Languages: SPANISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Over the last few years, there has been a considerable reduction in the mortality and morbidity associated with HIV patients, due to the use of protease inhibitors which have led to a true revolution in the treatment of this infection. A new problem has arisen with the increased life expectancy: the onset of a plurimetabolic syndrome characterized by hypertriglyceridaemia, hypercholesterolaemia and hyperglycaemia; in addition to anomalies in composition and distribution of body fat (central obesity and loss of peripheral fat) due to the associated lipodystrophy. As a result of the metabolic alterations, there is an increase in the risk of cardiovascular disease. Hyperglycaemia is the result of insulin resistance and is detected in between 13.6% and 46% of patients, possibly leading to type 2 diabetes (diagnosed in between 2.4% and 7% of the patients). These alterations have been documented as potentially related with the use of protease inhibitors and other drugs used in the handling of HIV patients. The appropriate treatment of altered metabolism of carbohydrate requires: 1) a customized dietary approach depending on individual BMI and lipid alterations; 2) a physical exercise programme; 3) the use of insulin sensitization drugs: metformin and thiazolidinediones and, where the therapeutic goals are not achieved or there is a contraindication for oral hypoglycaemic drugs; 4) insulin therapy with regimens similar to other diabetic patients. (34 Refs.)
Tags: Human
Descriptors: *Anti-HIV Agents--adverse effects--AE; *Carbohydrates --metabolism--ME; *HIV Infections--metabolism--ME; Acquired Immunodeficiency Syndrome--drug therapy--DT; Acquired Immunodeficiency Syndrome --metabolism--ME; Cardiovascular Diseases--epidemiology--EP; Diabetes Mellitus, Non-Insulin-Dependent--chemically induced--CI; Diabetes Mellitus, Non-Insulin-Dependent--diet therapy--DH; Diabetes Mellitus, Non-Insulin-Dependent--drug therapy--DT; Exercise Therapy; HIV Infections --drug therapy--DT; HIV Protease Inhibitors -- adverse effects --AE; Hypercholesterolemia--chemically induced--CI; Hypertriglyceridemia --chemically induced--CI; Hypoglycemic Agents--therapeutic use--TU; Incidence; Insulin--therapeutic use--TU; Insulin Resistance ; Lipodystrophy--chemically induced--CI; Metformin--therapeutic use--TU; Prevalence; Risk Factors; Thiazoles--therapeutic use--TU
CAS Registry No.: 0 (Anti-HIV Agents); 0 (Carbohydrates); 0 (HIV Protease Inhibitors); 0 (Hypoglycemic Agents); 0 (Thiazoles); 11061-68-0 (Insulin); 2295-31-0 (2,4-thiazolidinedione); 657-24-9 (Metformin)
Record Date Created: 20020801
Record Date Completed: 20021010

27/9/6
DIALOG(R)File 155:MEDLINE(R)
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10130496 22107973 PMID: 12132466
Side effects. Indinavir and insulin.
TreatmentUpdate (Canada) Aug 2000, 12 (5) p5, ISSN 1181-7186
Journal Code: 100891076
Document type: Newspaper Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIDS/HIV
Tags: Human; Male
Descriptors: HIV Protease Inhibitors -- adverse effects --AE; *Indinavir--adverse effects--AE; * Insulin Resistance ; Adult; Aged; HIV Seronegativity; Middle Age
CAS Registry No.: 0 (HIV Protease Inhibitors); 150378-17-9 (Indinavir)
Record Date Created: 20020711
Record Date Completed: 20020731

27/9/7
DIALOG(R)File 155:MEDLINE(R)
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10072981 22020256 PMID: 12025672
Metabolic complications of HIV and AIDs.
Briggs J M; Drabek C A
Department of Veterans Affairs Medical Center, Northern Ohio AIDS Education and Training Center, Cleveland, Ohio, USA.
Orthopaedic nursing / National Association of Orthopaedic Nurses (United States) Jul-Aug 2001, 20 (4) p41-50, ISSN 0744-6020 Journal Code: 8409486
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: NURSING
Numerous anecdotal reports, clinical observations, and newly published studies provide evidence of the growing interest and concern about body shape changes and metabolic complications seen in HIV infection. At first believed to be a single complication caused by the protease inhibitor class of antiretroviral therapy, the focus of research is shifting to distinct syndromes with multiple causes. In this unfolding story, peripheral fat atrophy, central fat accumulation, dyslipidemia, and glucose disregulation characterize the more commonly recognized syndromes. Osteoporosis and osteopenia have been recently observed. While the etiologies await discovery, the long-term consequences of these metabolic changes demand the expertise of clinicians not formerly considered "front-line" in HIV/AIDS treatment, such as orthopaedic nurses.
Tags: Human
Descriptors: *Acidosis, Lactic--chemically induced--CI; *HIV Infections --complications--CO; *Hyperlipidemia--chemically induced--CI; *Lipodystrophy--chemically induced--CI; Anticholesteremic Agents--therapeutic use--TU; HIV Infections--drug therapy--DT; HIV Infections--metabolism--ME; HIV Protease Inhibitors -- adverse effects --AE; Hyperlipidemia--drug therapy--DT; Insulin Resistance ; Reverse Transcriptase Inhibitors --adverse effects--AE
CAS Registry No.: 0 (Anticholesteremic Agents); 0 (HIV Protease Inhibitors); 0 (Reverse Transcriptase Inhibitors)
Record Date Created: 20020523
Record Date Completed: 20020624

27/9/8
DIALOG(R)File 155:MEDLINE(R)
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10040436 21977623 PMID: 11981359

Hypofibrinolytic state in HIV-1-infected patients treated with protease inhibitor-containing highly active antiretroviral therapy.

Koppel Kristina; Bratt Goran; Schulman Sam; Bylund Hakan; Sandstrom Eric
Venhalsan (Gay Men's Health Clinic), Karolinska Institute, Soder Hospital Stockholm, 118 83 Stockholm, Sweden. kristina.koppel@venh.sos.sll.se

Journal of acquired immune deficiency syndromes (1999) (United States) Apr 15 2002, 29 (5) p441-9, ISSN 1525-4135 Journal Code: 100892005
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV

Decreased insulin sensitivity, hyperlipidemia, and body fat changes are considered as risk factors for coronary heart disease (CHD). A clustering of such factors (metabolic syndrome [MSDR]) exponentially increases the risk. Impaired fibrinolysis and increased coagulation are additional independent risk factors for CHD. We studied the effects of protease inhibitor (PI)-containing highly active antiretroviral therapy (HAART) on metabolic and hemostatic parameters in 363 HIV-infected individuals, of whom 266 were receiving PI-containing HAART and 97 were treatment naive. The fasting plasma levels of insulin, glucose, triglycerides, cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, plasminogen activator inhibitor type 1 (PAI-1), and fibrinogen were evaluated together with the areas of visceral adipose tissue and the visceral adipose tissue/subcutaneous adipose tissue area ratio. The levels of insulin, triglycerides, cholesterol, and low-density lipoprotein cholesterol; visceral adipose tissue area; low-density lipoprotein/high-density lipoprotein ratio; and visceral adipose tissue/subcutaneous adipose tissue area ratio were significantly increased in patients receiving PI-containing HAART compared with treatment-naive patients. The levels of PAI-1 and fibrinogen were significantly higher in patients receiving PI-containing HAART. PAI-1 levels were higher in individuals with MSDR but also in patients without MSDR who were receiving PI-containing HAART. PAI-1 was independently correlated to use of PI-containing HAART, triglyceride level, insulin level, and body mass index ($p < .001$). These findings suggest that patients receiving PI-containing HAART have decreased fibrinolysis and increased coagulability, which may thus represent additional risk factors for cardiovascular disease in this patient group.

Tags: Human
Descriptors: Antiretroviral Therapy, Highly Active--adverse effects--AE; *Fibrinogen--analysis--AN; *HIV Infections--drug therapy--DT; * HIV Protease Inhibitors -- adverse effects --AE; *Plasminogen Activator Inhibitor 1--blood--BL; Adipose Tissue--metabolism--ME; Adult; Blood Glucose; C-Reactive Protein--analysis--AN; Cardiovascular Diseases --etiology--ET; Insulin Resistance ; Lipids--blood--BL; Lipodystrophy --etiology--ET; Middle Age; Risk Factors
CAS Registry No.: 0 (Blood Glucose); 0 (HIV Protease Inhibitors); 0 (Lipids); 0 (Plasminogen Activator Inhibitor 1); 9001-32-5 (Fibrinogen); 9007-41-4 (C-Reactive Protein)
Record Date Created: 20020430
Record Date Completed: 20020516

27/9/9
DIALOG(R)File 155:MEDLINE(R)
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09929489 21840569 PMID: 11858198
The latest word on lipodystrophy and mitochondrial toxicity (and old words that still resound).
Mascolini Mark
IAPAC monthly (United States) Jan 2002, 8 (1) p14-32,
Journal Code: 101087241
Document type: Newspaper Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIDS/HIV
Tags: Female; Human; Male
Descriptors: HIV Infections--complications--CO; * HIV Protease Inhibitors -- adverse effects --AE; *Lipodystrophy--etiology--ET; *Mitochondria--drug effects--DE; Antilipemic Agents--therapeutic use--TU; Bone Diseases, Metabolic--chemically induced--CI; DNA, Mitochondrial --analysis--AN; HIV Infections--drug therapy--DT; HIV Infections --physiopathology--PP; Hypoglycemic Agents--therapeutic use--TU; Insulin --blood--BL; Insulin Resistance ; Lipodystrophy--chemically induced--CI; Lipodystrophy--drug therapy--DT; Reverse Transcriptase Inhibitors--adverse effects--AE; Reverse Transcriptase Inhibitors--therapeutic use--TU
CAS Registry No.: 0 (Antilipemic Agents); 0 (DNA, Mitochondrial); 0 (HIV Protease Inhibitors); 0 (Hypoglycemic Agents); 0 (Reverse Transcriptase Inhibitors); 11061-68-0 (Insulin)
Record Date Created: 20020219
Record Date Completed: 20020228

27/9/10
DIALOG(R)File 155:MEDLINE(R)
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09849446 21661290 PMID: 11802627
Metabolic complications of HIV infection: translating research findings into clinical practice.
Currier Judith
AIDS clinical care (United States) Jan 2002, 14 (1) p1-2, 8, ISSN 1043-1543 Journal Code: 9000367
Document type: Editorial; Newspaper Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIDS/HIV
The editors of ACC recognize that our coverage of the topic of metabolic complications is unable to address all of the issues that clinicians face on a daily basis. The absence of information to guide clinicians on the management of lipoatrophy, fat accumulation, avascular necrosis, and breast enlargement is a reflection of the limitations of current data, not a statement about the importance of these topics. As new data emerge in these areas we will strive to keep our readers informed. Much work remains to be done in defining the causes of, and treatments for, the metabolic complications of HIV infection. For starters, a more critical assessment of the metabolic profiles of each of the available antiretroviral agents--or, at a minimum, an understanding of their impact on lipid levels and glucose metabolism in treatment-naive patients--is long overdue. Although it is clearly not possible to examine all of the potential combinations of the available agents in equal depth, some basic information about all of the FDA-approved drugs should be developed. Only through careful study of the underlying mechanisms by which these agents contribute to the development of the myriad of metabolic abnormalities will we be able to develop new agents and optimal management strategies for people living with HIV infection.
Tags: Human
Descriptors: *HIV Infections--complications--CO; *Metabolic Diseases --complications--CO; Bone Diseases, Metabolic--complications--CO; Drug Therapy, Combination; HIV Infections--drug therapy--DT; HIV Protease Inhibitors -- adverse effects --AE; Hyperlipidemia--complications--CO; Insulin Resistance ; Lipodystrophy--complications--CO; Reverse Transcriptase Inhibitors--adverse effects--AE
CAS Registry No.: 0 (HIV Protease Inhibitors); 0 (Reverse Transcriptase Inhibitors)
Record Date Created: 20020122
Record Date Completed: 20020213

27/9/11
DIALOG(R)File 155:MEDLINE(R)
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09842900 21654201 PMID: 11794859
Sugar blues and protease inhibitors.
TreatmentUpdate (Canada) Nov-Dec 2001, 13 (7) p4, ISSN 1181-7186
Journal Code: 100891076
Document type: Newspaper Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIDS/HIV
Tags: Human
Descriptors: Diabetes Mellitus, Non-Insulin-Dependent--chemically induced --CI; * HIV Protease Inhibitors -- adverse effects --AE; *Indinavir --adverse effects--AE; Blood Glucose--analysis--AN; Clinical Trials; Diabetes Mellitus, Non-Insulin-Dependent--drug therapy--DT; HIV Seronegativity; Hypoglycemic Agents--therapeutic use--TU; Insulin Resistance ; Placebos
CAS Registry No.: 0 (Blood Glucose); 0 (HIV Protease Inhibitors); 0 (Hypoglycemic Agents); 0 (Placebos); 150378-17-9 (Indinavir)
Record Date Created: 20020117
Record Date Completed: 20020201

27/9/12
DIALOG(R)File 155:MEDLINE(R)
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09693407 21485795 PMID: 11600828

Fat distribution and metabolic changes are strongly correlated and energy expenditure is increased in the HIV lipodystrophy syndrome.

Kosmiski L A; Kuritzkes D R; Lichtenstein K A; Glueck D H; Gourley P J; Stamm E R; Scherzinger A L; Eckel R H

Division of Endocrinology, Metabolism and Diabetes, University of Colorado Health Sciences Center, Denver, Colorado, USA.

AIDS (London, England) (England) Oct 19 2001, 15 (15) p1993-2000, ISSN 0269-9370 Journal Code: 8710219

Contract/Grant No.: K23 RR16069; RR; NCRR; K24 RR16482; RR; NCRR; M01RR0051; RR; NCRR

Comment in AIDS. 2001 Oct 19;15(15) 2037-41; Comment in PMID 11600834

Document type: Clinical Trial; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS; AIDS/HIV

OBJECTIVE: To examine the relationships between protease inhibitor (PI) therapy, body fat distribution and metabolic disturbances in the HIV lipodystrophy syndrome. DESIGN: Cross-sectional study. SETTING: HIV primary care practices. PATIENTS: PI-treated patients with lipodystrophy (n= 14) and PI-treated (n= 13) and PI-naive (n= 5) patients without lipodystrophy. MAIN OUTCOME MEASURES: Body composition was assessed by physical examination, dual-energy X-ray absorptiometry and computed tomography. Insulin sensitivity (SI) was measured using the insulin-modified frequently sampled intravenous glucose tolerance test. Lipid profiles, other metabolic parameters, duration of HIV infection, CD4 lymphocyte counts, HIV-1 RNA load and resting energy expenditure (REE) were also assessed. RESULTS: PI-treated patients with lipodystrophy were significantly less insulin sensitive than PI-treated patients and PI-naive patients without any changes in fat distribution (SI(22) x 10(-4) (min(-1)/microU/ml) versus 3.2 x 10(-4) and 4.6 x 10(-4) (min(-1)/microU/ml), respectively; $P < 0.001$). Visceral adipose tissue area and other measures of central adiposity correlated strongly with metabolic disturbances as did the percent of total body fat present in the extremities; visceral adipose tissue was an independent predictor of insulin sensitivity and high density lipoprotein cholesterol levels. REE per kg lean body mass was significantly higher in the group with lipodystrophy compared to the groups without lipodystrophy (36.9 versus 31.5 and 29.4 kcal/kg lean body mass; $P < 0.001$), and SI was strongly correlated with and was an independent predictor of REE in this population. CONCLUSIONS: Body fat distribution and metabolic disturbances are strongly correlated in the HIV lipodystrophy syndrome and REE is increased.

Tags: Female; Human; Male; Support, U.S. Gov't, P.H.S.

Descriptors: Adipose Tissue--physiology--PH; *Anti-HIV Agents--adverse effects--AE; *Energy Metabolism; *HIV Infections--complications--CO; * HIV Protease Inhibitors -- adverse effects --AE; *Lipodystrophy --metabolism--ME; Adult; Body Composition; CD4 Lymphocyte Count; Cross-Sectional Studies; Glucose Tolerance Test--methods--MT; HIV Infections--drug therapy--DT; HIV-1--physiology--PH; Insulin Resistance ; Lipodystrophy--chemically induced--CI; Lipodystrophy--physiopathology --PP; Middle Age; RNA, Viral--blood--BL; Viral Load

CAS Registry No.: 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors); 0 (RNA, Viral)

Record Date Created: 20011015

Record Date Completed: 20020103

27/9/13
DIALOG(R)File 155:MEDLINE(R)
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09672153 21462179 PMID: 11579243
HIV protease inhibitor substitution in patients with lipodystrophy: a randomized, controlled, open-label, multicentre study.
Carr A; Hudson J; Chuah J; Mallal S; Law M; Hoy J; Doong N; French M; Smith D; Cooper D A
HIV, Immunology and Infectious Disease Clinical Services Unit, St. Vincent's Hospital, Sydney, Australia.
AIDS (London, England) (England) Sep 28 2001, 15 (14) p1811-22, ISSN 0269-9370 Journal Code: 8710219
Document type: Clinical Trial; Journal Article; Multicenter Study; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
BACKGROUND: Lipodystrophy, dyslipidaemia and insulin resistance often complicate protease inhibitor-containing antiretroviral therapy. The aims of this study were to determine if these are reversible with continued HIV suppression following protease inhibitor substitution. METHODS: Eighty-one HIV protease inhibitor recipients (78 male; mean antiretroviral therapy, 55 months) with predominant peripheral lipoatrophy, HIV RNA < 400 copies/ml plasma for at least the preceding 6 months, and no prior abacavir, non-nucleoside analogue or adefovir therapy were randomized 3 : 2 to continue nucleoside analogues and substitute protease inhibitor(s) with abacavir, nevirapine, adefovir and hydroxyurea (n = 49) or to continue all therapy (n = 32) with an option to switch at week 24. The primary endpoints were total body fat and HIV RNA at week 24. Other assessments were regimen safety, regional body composition, metabolic parameters, quality of life, and CD4 T-lymphocyte counts to week 48. RESULTS: There was a greater decline in total body fat in the switch group than in the continue group (-1.6 and -0.4 kg, respectively at week 24; P = 0.006). This comprised greater declines in limb and subcutaneous abdominal fat, and in intra-abdominal fat of patients with moderate or severe abdominal fat accumulation. Viral suppression was similar, despite 18 (37%) switch group patients ceasing at least one study drug by week 24 because of adverse events. Total cholesterol and triglycerides declined more in the switch group (both P < 0.002). High density lipoprotein cholesterol increased significantly in both groups at week 48 (P < 0.02). There was no change for any glycaemic parameter. CONCLUSIONS: In predominantly lipoatrophic patients, switching from HIV protease inhibitor therapy lead to improved lipids and less intra-abdominal fat, but also to less peripheral fat, and had minimal effect on insulin resistance. Virological control in these heavily pretreated patients was unaffected, despite frequent switch drug cessations.
Tags: Female; Human; Male; Support, Non-U.S. Gov't
Descriptors: *Adenine--analogs and derivatives--AA; *Anti-HIV Agents --therapeutic use--TU; *Antiretroviral Therapy, Highly Active; *HIV Infections--drug therapy--DT; *Lipodystrophy--chemically induced--CI; *Reverse Transcriptase Inhibitors--therapeutic use--TU; Adenine --therapeutic use--TU; Body Composition; Carnitine--therapeutic use--TU; Dideoxynucleosides--therapeutic use--TU; Drug Administration Schedule; HIV Infections--immunology--IM; HIV Infections--virology--VI; HIV Protease Inhibitors -- adverse effects --AE; HIV Protease Inhibitors --therapeutic use--TU; HIV-1--physiology--PH; Hydroxyurea--therapeutic use --TU; Insulin Resistance ; Lipodystrophy--drug therapy--DT; Middle Age; Nevirapine--therapeutic use--TU; Quality of Life; RNA, Viral--blood--BL; Treatment Outcome
CAS Registry No.: 0 (Anti-HIV Agents); 0 (Dideoxynucleosides); 0 (HIV Protease Inhibitors); 0 (RNA, Viral); 0 (Reverse Transcriptase Inhibitors); 0 (abacavir); 106941-25-7 (9-(2-phosphonylmethoxyethyl)adenine); 127-07-1 (Hydroxyurea); 129618-40-2 (Nevirapine); 541-15-1 (Carnitine); 73-24-5 (Adenine)
Record Date Created: 20011001
Record Date Completed: 20011214

27/9/14
DIALOG(R)File 155:MEDLINE(R)
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09665239 21454882 PMID: 11570289
Background on glucose--from food to blood sugar.
TreatmentUpdate (Canada) Jun 2001, 13 (2) p7, ISSN 1181-7186
Journal Code: 100891076
Document type: Newspaper Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIDS/HIV
Tags: Human
Descriptors: *Blood Glucose; *Glucose; Anti-HIV Agents--adverse effects --AE; HIV Protease Inhibitors -- adverse effects --AE; Indinavir --adverse effects--AE; Insulin--physiology--PH; Insulin Resistance
CAS Registry No.: 0 (Anti-HIV Agents); 0 (Blood Glucose); 0 (HIV Protease Inhibitors); 11061-68-0 (Insulin); 150378-17-9 (Indinavir); 50-99-7 (Glucose)
Record Date Created: 20010925
Record Date Completed: 20011018

27/9/15
DIALOG(R)File 155:MEDLINE(R)
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09608274 21393208 PMID: 11501201
Effects of sex and race on lipodystrophy pathogenesis.
Nolan D; Mallal S
Centre for Clinical Immunology and Biomedical Statistics, Level 2, North Block Royal Perth Hospital, Wellington Street, Western Australia, 6000, Australia.
Journal of HIV therapy (England) May 2001, 6 (2) p32-6, ISSN 1462-0308 Journal Code: 101088049
Comment in J HIV Ther. 2001 May;6(2) 25-7; Comment in PMID 11501199
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
(44 Refs.)
Tags: Female; Human; Male
Descriptors: Antiretroviral Therapy, Highly Active--adverse effects--AE; *HIV Infections--drug therapy--DT; * HIV Protease Inhibitors -- adverse effects --AE; *Lipodystrophy--ethnology--EH; *Lipodystrophy--etiology --ET; Adipose Tissue--anatomy and histology--AH; Cardiovascular Diseases --etiology--ET; Hyperlipidemia--complications--CO; Insulin Resistance ; Lipodystrophy--chemically induced--CI; Lipodystrophy--pathology--PA; Risk Factors; Sex Factors
CAS Registry No.: 0 (HIV Protease Inhibitors)
Record Date Created: 20010814
Record Date Completed: 20010906

27/9/16
DIALOG(R)File 155:MEDLINE(R)
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09559788 21341458 PMID: 11448728
Metabolic complications associated with antiretroviral therapy.
Jain R G; Furfine E S; Pedneault L; White A J; Lenhard J M
Department of Metabolic Diseases, GlaxoSmithKline Inc., 5 Moore Drive, 27709, Research Triangle Park, NC, USA.
Antiviral research (Netherlands) Sep 2001, 51 (3) p151-77, ISSN 0166-3542 Journal Code: 8109699
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Mortality rates in the HIV-infected patient population have decreased with the advent of highly active antiretroviral therapy (HAART) for the treatment of AIDS. Due to the chronic nature of HAART, long-term metabolic complications are associated with therapy, such as hyperlipidemia, fat redistribution and diabetes mellitus. Currently, all of these symptoms are classified as the lipodystrophy (LD) syndrome(s). However, hyperlipidemia and fat redistribution occur independently, indicating there may be multiple syndromes associated with HAART. Although fat gain/loss and dyslipidemia occur in protease inhibitor (PI) naive patients treated with nucleoside reverse transcriptase inhibitors (NRTIs), combination therapies (PI and NRTI) accelerate the syndrome. Recent clinical trials, cell culture and animal studies indicate that these effects are not drug class specific and select PIs, NRTIs and non-nucleoside reverse transcriptase inhibitors (NNRTIs) can be associated with metabolic complications. Moreover, the effects can vary between various members of the same class of antiretroviral agents (i.e. not all PIs cause the same adverse reactions) and may be influenced by duration of infection, genetics and environmental factors. Although HAART increases the risk of metabolic complications, this does not outweigh the benefits of survival. In this review, we summarize the latest clinical and scientific information on these metabolic complications, examine current hypotheses explaining the syndromes and comment on the existing methods available to manage these metabolic side effects. (150 Refs.)
Tags: Human
Descriptors: *Antiretroviral Therapy, Highly Active--adverse effects--AE; *HIV Infections--drug therapy--DT; *Lipodystrophy--chemically induced--CI; Diabetes Mellitus--chemically induced--CI; Glucose--metabolism--ME; HIV Protease Inhibitors -- adverse effects --AE; Hyperlipidemia --chemically induced--CI; Insulin Resistance ; Reverse Transcriptase Inhibitors--adverse effects--AE; Risk Factors; Syndrome
CAS Registry No.: 0 (HIV Protease Inhibitors); 0 (Reverse Transcriptase Inhibitors); 50-99-7 (Glucose)
Record Date Created: 20010712
Record Date Completed: 20010920

27/9/17
DIALOG(R)File 155:MEDLINE(R)
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09365343 21127661 PMID: 11224652
Hyperlipidemia and inhibitors of HIV protease.
Distler O; Cooper D A; Deckelbaum R J; Sturley S L
Institute of Human Nutrition, Columbia University College of Physicians and Surgeons, New York, NY 10032, USA.
Current opinion in clinical nutrition and metabolic care (England) Mar 2001, 4 (2) p99-103, ISSN 1363-1950 Journal Code: 9804399
Contract/Grant No.: HL40404; HL; NHLBI; P30 AI42848; AI; NIAID
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
HIV protease inhibitors have been successfully incorporated into therapy for patients with HIV. These otherwise efficacious treatments present with multiple metabolic side-effects and body habitus changes known as the lipodystrophy syndrome. Direct associations of the lipid abnormalities with protease inhibitor use have been described, and ongoing studies are focused on describing mechanisms for future intervention. Mechanisms based on the molecular identity of the protease inhibitor target with human proteins, interference with aspects critical to lipoprotein production, and interference with adipocyte differentiation have been described. This review highlights the complexities of this syndrome, and discusses putative mechanisms whereby protease inhibitors cause hyperlipidemia. (47 Refs.)
Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Descriptors: HIV Infections--drug therapy--DT; * HIV Protease Inhibitors -- adverse effects --AE; *Hyperlipidemia--etiology--ET; *Lipodystrophy--chemically induced--CI; Adipocytes--metabolism--ME; HIV Protease Inhibitors--pharmacokinetics--PK; HIV Protease Inhibitors --therapeutic use--TU; Insulin Resistance ; Lipids--blood--BL; Lipodystrophy--metabolism--ME
CAS Registry No.: 0 (HIV Protease Inhibitors); 0 (Lipids)
Record Date Created: 20010306
Record Date Completed: 20010726

27/9/18
DIALOG(R)File 155:MEDLINE(R)
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09273426 21010241 PMID: 11126425
Metabolic disorders among HIV-infected patients treated with protease inhibitors: a review.
Graham N M
Virco Group NV, Durham, North Carolina 27713, USA.
Journal of acquired immune deficiency syndromes (1999) (United States)
Oct 1 2000, 25 Suppl 1 pS4-11, ISSN 1525-4135 Journal Code: 100892005
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
Currently available protease inhibitors are associated with development of a group of metabolic disorders. These include a peripheral lipodystrophy syndrome in which there is fat wasting in the face, arms, and legs; fat accumulation in the abdomen, dorsocervical region, and/or breasts (women only); as well as hyperlipidemia, hypercholesterolemia, and insulin resistance. A review of 15 observational studies and case reports shows that the incidence of the peripheral lipodystrophy syndrome increases with time of exposure to protease inhibitors, with a >60% incidence seen after 1 year of continuous treatment. Protease inhibitors are hypothesized to cause this syndrome by impairing conversion of retinoic acid to cis-9-retinoic acid (leading to impaired peripheral fat storage, sequestration of body fat to central adipocytes, and hyperlipidemia) and by inhibiting low-density lipoprotein receptor-related protein (LRP), thus preventing postprandial chylomicron clearance and further contributing to hyperlipidemia. Recent in vitro data suggest that more than one pathway contributes to the lipodystrophy syndrome and that pathways may differ among protease inhibitors. Although the central fat accumulation, hyperlipidemia, and insulin resistance components of this syndrome may reverse after discontinuation of protease inhibitor therapy, it is not known whether complete normalization of fast-wasted body regions is possible. Prospective controlled studies are needed to define whether protease inhibitors currently under development are less prone to produce the lipodystrophy syndrome. (37 Refs.)
Tags: Female; Human; Male
Descriptors: HIV Infections--complications--CO; * HIV Protease Inhibitors -- adverse effects --AE; *HIV-1; *Lipodystrophy--chemically induced--CI; *Lipodystrophy--epidemiology--EP; Drug Therapy, Combination; HIV Infections--drug therapy--DT; HIV Infections--virology--VI; Hyperlipidemia--chemically induced--CI; Insulin Resistance ; Reverse Transcriptase Inhibitors--therapeutic use--TU
CAS Registry No.: 0 (HIV Protease Inhibitors); 0 (Reverse Transcriptase Inhibitors)
Record Date Created: 20001220
Record Date Completed: 20010111

27/9/19
DIALOG(R)File 155:MEDLINE(R)
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09268239 20700655 PMID: 11366793
Transfer therapy--Nevirapine for protease problems?
TreatmentUpdate (CANADA) Jun 01 1999, 11 (4) p6-7, ISSN 1181-7186
Journal Code: 100891076
Document type: Newspaper Article
Languages: ENGLISH, FRENCH
Main Citation Owner: NLM
Abstract Source: AIDS
Record type: Completed
Subfile: AIDS/HIV
A study by doctors in Spain found that people taking antiviral therapy may develop higher-than-normal levels of lipids and glucose in their blood, insulin resistance, and body shape changes due to fat redistribution. Switching to Nevirapine (Viramune) from a protease-based regimen reversed these side effects in 6 months, and levels of CD4+ and viral load remained unchanged in most subjects. Although lab measures were improved, body shape did not return completely to its pre-protease shape in any of the subjects.
Tags: Female; Human; Male
Descriptors: HIV Infections--drug therapy--DT; *HIV Infections --metabolism--ME; * HIV Protease Inhibitors -- adverse effects --AE; *Nevirapine--therapeutic use--TU; *Reverse Transcriptase Inhibitors --therapeutic use--TU; Adipose Tissue--metabolism--ME; Anthropometry; Blood Glucose--metabolism--ME; CD4 Lymphocyte Count; Cholesterol--blood--BL; Drug Therapy, Combination; HIV Infections--virology--VI; HIV Protease Inhibitors --therapeutic use--TU; HIV-1--drug effects--DE; HIV-1--physiology--PH; Insulin Resistance ; Triglycerides--blood--BL; Viral Load
CAS Registry No.: 0 (Blood Glucose); 0 (HIV Protease Inhibitors); 0 (Reverse Transcriptase Inhibitors); 0 (Triglycerides); 129618-40-2 (Nevirapine); 57-88-5 (Cholesterol)
Record Date Created: 20000607
Record Date Completed: 20000607

27/9/20
DIALOG(R)File 155:MEDLINE(R)
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09268238 20700654 PMID: 11366792
Protease therapy and changes to insulin and glucose.
TreatmentUpdate (CANADA) Jun 01 1999, 11 (4) p5-6, ISSN 1181-7186
Journal Code: 100891076
Document type: Newspaper Article
Languages: ENGLISH, FRENCH
Main Citation Owner: NLM
Abstract Source: AIDS
Record type: Completed
Subfile: AIDS/HIV

A study by doctors in Germany found that HIV-infected people who received PI therapy were more likely to have problems with their body's ability to use glucose. PI use was associated with reduced insulin sensitivity, and the development of diabetes in severe cases. In addition, PI treated subjects had increased levels of lipids in the blood, specifically triglycerides and cholesterol. These levels were not linked to the amount of time people used PIs.

Tags: Female; Human; Male
Descriptors: Glucose Tolerance Test; *HIV Infections--drug therapy--DT; * HIV Protease Inhibitors -- adverse effects --AE; *HIV-1; *Insulin --blood--BL; * Insulin Resistance ; Adult; Aged; Cholesterol--blood--BL; HIV Infections--blood--BL; HIV Infections--physiopathology--PP; HIV Protease Inhibitors--therapeutic use--TU; Middle Age; Triglycerides--blood --BL
CAS Registry No.: 0 (HIV Protease Inhibitors); 0 (Triglycerides); 11061-68-0 (Insulin); 57-88-5 (Cholesterol)
Record Date Created: 20000607
Record Date Completed: 20000607

27/9/21
DIALOG(R)File 155:MEDLINE(R)
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09267824 20700240 PMID: 11366378
IDSA '98 highlights.
HIV hotline (UNITED STATES) Dec 1998, 8 (5-6) p1, 6-7, 9,
Journal Code: 9200421
Document type: Congresses; Newspaper Article
Languages: ENGLISH
Main Citation Owner: NLM
Abstract Source: AIDS
Record type: Completed
Subfile: AIDS/HIV

The annual meeting of the Infectious Diseases Society of America (IDSA) focused on reasons for HIV treatment failure, modification of failed treatment, and costs and adverse effects of therapy. Featured were studies on virological rebound during antiretroviral therapy and hormonal therapy given to patients exhibiting lipodystrophy-associated body changes. More than 90% of HIV-positive individuals display evidence of previous herpes simplex virus (HSV) infection. A correlation drawn between the acquisition of HSV-2 and HIV through sexual contact indicated HSV-2 may play a role in the transmission of HIV. Rising treatment costs by newer anti-HIV therapies are offset by lower expenses for nondrug medical services.

Tags: Human
Descriptors: *Anti-HIV Agents--therapeutic use--TU; *HIV Infections --complications--CO; *HIV Infections--drug therapy--DT; *Hyperlipidemia --etiology--ET; *Lipodystrophy--etiology--ET; Anti-HIV Agents --adverse effects--AE; Anti-HIV Agents--economics--EC; Drug Resistance, Microbial; Drug Therapy, Combination; HIV Infections--transmission--TM; HIV Protease Inhibitors -- adverse effects --AE; Health Services Accessibility; Herpes Simplex--complications--CO; Herpesviridae Infections --complications--CO; Herpesviridae Infections--epidemiology--EP; Insulin Resistance ; RNA, Viral--blood--BL; Syndrome; Ulcer--complications--CO; Viral Load
CAS Registry No.: 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors); 0 (RNA, Viral)
Record Date Created: 20000412
Record Date Completed: 20000412

27/9/22
DIALOG(R)File 155:MEDLINE(R)
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09267650 20700066 PMID: 11366205
Fat, sugar and drugs on the French Riviera.
Lands L
GMHC treatment issues - the Gay Men's Health Crisis newsletter of experimental AIDS therapies (UNITED STATES) Mar 1999, 13 (3) p9-11, ISSN 1077-1824 Journal Code: 9509489
Document type: Newspaper Article
Languages: ENGLISH
Main Citation Owner: NLM
Abstract Source: AIDS
Record type: Completed
Subfile: AIDS/HIV
The 3rd International Conference on Nutrition and HIV Infection emphasized lipodystrophy and the metabolic implications of highly active antiretroviral therapy (HAART). Several presentations challenged the idea that protease inhibitors alone caused lipodystrophy. The way lipodystrophy manifests itself appears to differ by gender; study results were described. The impact of dietary fat on elevated blood lipids was also discussed. The use of human growth hormone as a treatment was explored.
Tags: Female; Human; Male
Descriptors: Anti-HIV Agents--adverse effects--AE; *HIV Infections --complications--CO; * HIV Protease Inhibitors -- adverse effects --AE; *Lipids--blood--BL; *Lipodystrophy--chemically induced--CI; *Osteoporosis--etiology--ET; Anti-HIV Agents--therapeutic use--TU; Body Composition; Bone Density; Diet, Reducing; Drug Therapy, Combination; Exercise; Growth Hormone--therapeutic use--TU; HIV Infections--drug therapy --DT; HIV Protease Inhibitors--therapeutic use--TU; Hyperlipidemia --prevention and control--PC; Hypoglycemic Agents--therapeutic use--TU; Insulin Resistance ; Lipodystrophy--epidemiology--EP; Lipodystrophy --prevention and control--PC; Osteoporosis--epidemiology--EP; Sex Factors
CAS Registry No.: 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors); 0 (Hypoglycemic Agents); 0 (Lipids); 9002-72-6 (Growth Hormone)
Record Date Created: 20000121
Record Date Completed: 20000121

27/9/23
DIALOG(R)File 155:MEDLINE(R)
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09236640 20549066 PMID: 11096014

Disorders of glucose metabolism in patients infected with human immunodeficiency virus.

Dube M P

Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, USA. mpdube@iupui.edu

Clinical infectious diseases - an official publication of the Infectious Diseases Society of America (UNITED STATES) Dec 2000, 31 (6) p1467-75, ISSN 1058-4838 Journal Code: 9203213

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

New-onset diabetes mellitus, clinically similar to type 2 diabetes, will affect a small proportion (1%-6%) of patients infected with human immunodeficiency virus (HIV) who are treated with HIV-1 protease inhibitors (PIs). However, insulin resistance and impaired glucose tolerance will develop during PI treatment in a considerable proportion of patients. Dyslipidemia, abdominal obesity, and loss of peripheral fat frequently coexist with insulin resistance, but it is not clear whether all of these result from a common pathogenic mechanism. Recent data suggest that insulin resistance may also be associated with HIV infection in patients not receiving PI therapy. The long-term consequences of insulin resistance in this population are not known. The effect of switching to other antiretroviral therapies has not been fully determined. Treatment of established diabetes mellitus should generally follow existing guidelines. There is no clinically useful screening test that will determine the existence and degree of insulin resistance in individual patients. It is therefore reasonable to recommend general measures to increase insulin sensitivity in all patients infected with HIV, such as weight reduction for obese persons and regular aerobic exercise. (83 Refs.)

Tags: Human

Descriptors: Anti-HIV Agents--adverse effects--AE; *Glucose--metabolism --ME; *HIV Infections--complications--CO; *HIV Infections--drug therapy --DT; * HIV Protease Inhibitors -- adverse effects --AE; Anti-HIV Agents--therapeutic use--TU; Diabetes Mellitus--diagnosis--DI; Diabetes Mellitus--etiology--ET; Glucose Tolerance Test; HIV Infections--metabolism --ME; HIV Protease Inhibitors--therapeutic use--TU; Insulin Resistance

CAS Registry No.: 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors); 50-99-7 (Glucose)

Record Date Created: 20010202

Record Date Completed: 20010426

27/9/24
DIALOG(R)File 155:MEDLINE(R)
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09149454 20451440 PMID: 10996887
[Changes in lipid metabolism of patients infected by human immunodeficiency virus. A pathogenic hypothesis]
Alteraciones del metabolismo de los lipidos en los pacientes infectados por el virus de la inmunodeficiencia humana. Una hipotesis acerca de su patogenia.
Rodriguez Vidigal F F; Munoz Sanz A
Departamento de Medicina Interna, Hospital Universitario Infanta Cristina, Insalud-Universidad de Extremadura, Badajoz.
Medicina clinica (SPAIN) Jun 24 2000, 115 (4) p145-50, ISSN 0025-7753 Journal Code: 0376377
Document type: Journal Article; Review; Review, Tutorial
Languages: SPANISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
(77 Refs.)
Tags: Comparative Study; Female; Human; Male
Descriptors: *HIV Infections--metabolism--ME; *HIV Wasting Syndrome --etiology--ET; *Lipids--metabolism--ME; *Lipodystrophy--etiology--ET; Acquired Immunodeficiency Syndrome--metabolism--ME; Anti-HIV Agents --adverse effects--AE; Cardiovascular Diseases--etiology--ET; Fats --metabolism--ME; HIV Infections--complications--CO; HIV Infections--drug therapy--DT; HIV Protease Inhibitors -- adverse effects --AE; HIV Wasting Syndrome--chemically induced--CI; Hyperglycemia--etiology--ET; Hyperglycemia--metabolism--ME; Hyperlipoproteinemia--etiology--ET; Hyperl ipoproteinemia--metabolism--ME; Insulin Resistance ; Lipodystrophy --chemically induced--CI; Lipodystrophy--genetics--GE; Lipodystrophy --therapy--TH; Reverse Transcriptase Inhibitors--adverse effects--AE; Risk Factors
CAS Registry No.: 0 (Anti-HIV Agents); 0 (Fats); 0 (HIV Protease Inhibitors); 0 (Lipids); 0 (Reverse Transcriptase Inhibitors)
Record Date Created: 20001017
Record Date Completed: 20001017

27/9/25
DIALOG(R)File 155:MEDLINE(R)
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09148237 20450203 PMID: 10997397
Metabolic and anthropometric consequences of interruption of highly active antiretroviral therapy.
Hatano H; Miller K D; Yoder C P; Yanovski J A; Sebring N G; Jones E C; Davey R T
Laboratory of Immunoregulation, National Institute of Allergy and Infectious Diseases, National Institute of Health, Bethesda, Maryland 20892-1880, USA.
AIDS (London, England) (ENGLAND) Sep 8 2000, 14 (13) p1935-42, ISSN 0269-9370 Journal Code: 8710219
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
BACKGROUND: HAART has been associated with metabolic abnormalities (hyperlipidemia, insulin resistance, alterations in cortisol metabolism) and fat redistribution. SETTING: A prospective study of 26 Caucasian men (median age 43.5 years) with HIV-1 viral loads < 500 copies/ml for 12 months while on highly active antiretroviral therapy (HAART) who interrupted treatment for a median of 7.0 weeks (range 4.9-10.3 weeks). Seventeen (65.4%) patients reported at least one fat redistribution symptom at baseline. METHOD: Serum lipids, glucose and insulin levels during an oral glucose tolerance test, 24-h urinary free cortisol and 17-hydroxycorticosteroids, and anthropometric parameters were measured before HAART cessation and prior to its reinstitution. RESULTS: When baseline values were compared with those obtained after HAART interruption (means +/- SD), there was a significant decrease in total cholesterol (194+/-47.3 versus 159+/-29.3 mg/dl; P < 0.0001), low density lipoprotein (LDL) cholesterol (114+/-32.6 versus 96+/-24.7 mg/dl; P = 0.0013), triglycerides (261+/-244.3 versus 185+/-165.4 mg/dl; P = 0.008), and 24-hour urinary 17-hydroxycorticosteroids (15+/-7.9 versus 5+/-2.5 mg/24 h, P < 0.0001) and a significant increase in 24-hour urinary free cortisol (45+/-34.1 versus 62+/-32.2 microg/24 h; P = 0.016). There were no significant changes in glucose or insulin levels or in anthropometric measurements. CONCLUSIONS: A relatively brief interruption of HAART resulted in significant improvements in total cholesterol, LDL cholesterol, and triglyceride levels. No changes were observed in insulin resistance profiles or anthropometric measurements, perhaps because of the brief duration of HAART interruption. These results suggest that hyperlipidemia and alterations in corticosteroid metabolism in the setting of HAART are a direct drug effect that reverses with drug withdrawal. However, glucose metabolism and fat redistribution do not change over the short term.
Tags: Human; Male
Descriptors: Antiretroviral Therapy, Highly Active; *Body Composition; *HIV Infections--drug therapy--DT; * Insulin Resistance ; *Lipids--blood --BL; Adult; Antiretroviral Therapy, Highly Active--adverse effects--AE; Cholesterol--blood--BL; HIV Infections--immunology--IM; HIV Infections --metabolism--ME; HIV Infections--virology--VI; HIV Protease Inhibitors --administration and dosage--AD; HIV Protease Inhibitors -- adverse effects --AE; HIV Protease Inhibitors--therapeutic use--TU; Hydrocortisone--urine--UR; Hypercholesterolemia--chemically induced--CI; Hyperlipidemia--chemically induced--CI; Lipodystrophy--chemically induced --CI; Middle Age; Prospective Studies; Reverse Transcriptase Inhibitors --administration and dosage--AD; Reverse Transcriptase Inhibitors--adverse effects--AE; Reverse Transcriptase Inhibitors--therapeutic use--TU; Skinfold Thickness; Triglycerides--blood--BL
CAS Registry No.: 0 (HIV Protease Inhibitors); 0 (Lipids); 0 (Reverse Transcriptase Inhibitors); 0 (Triglycerides); 50-23-7 (Hydrocortisone); 57-88-5 (Cholesterol)
Record Date Created: 20001221
Record Date Completed: 20010208

27/9/26
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09085383 20382589 PMID: 10922955
[Metabolic complications associated with use of protease inhibitors]
Problemes metaboliques observes sous traitement par antiproteases.
Mosnier-Pudar H
Service des Maladies Endocrines et Metaboliques, Hopital Cochin, 27, rue du Faubourg-Saint-Jacques, 75014 Paris.
Annales de medecine interne (FRANCE) Jun 2000, 151 (4) p278-82, ISSN 0003-410X Journal Code: 0171744
Document type: Journal Article; Review; Review, Tutorial ; English Abstract
Languages: FRENCH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
The potency of highly active antiretroviral therapy, including protease inhibitors have led to declining morbidity and mortality in patients with HIV infection. However the use of protease inhibitors is associated with onset of morphologic and metabolic disorders. A syndrome of lipodystrophy has been described. It is characterized by fast wasting of the face and limbs, and a central adiposity, breast hypertrophy and buffalo neck. The prevalence of lipodystrophy in patients treated with protease inhibition is about 60%. The principal metabolic disorders are lipid abnormalities, principally hypertriglyceridemia. New onset of diabetes mellitus is less frequent. The pathogenesis of these abnormalities unknown. Insulin resistance seems to be a common feature of protease inhibitor associated metabolic an morphologic side-effects. (26 Refs.)
Tags: Human
Descriptors: Diabetes Mellitus--chemically induced--CI; * HIV Protease Inhibitors -- adverse effects --AE; *Hypertriglyceridemia--chemically induced--CI; *Lipodystrophy--chemically induced--CI; Diabetes Mellitus --epidemiology--EP; Diabetes Mellitus--metabolism--ME; Hyperglycemia --chemically induced--CI; Hyperglycemia--epidemiology--EP; Hyperglycemia --metabolism--ME; Hypertriglyceridemia--epidemiology--EP; Hypertriglyceridemia--metabolism--ME; Insulin Resistance ; Lipodystrophy--epidemiology --EP; Lipodystrophy--metabolism--ME; Prevalence
CAS Registry No.: 0 (HIV Protease Inhibitors)
Record Date Created: 20001012
Record Date Completed: 20001012

27/9/27
DIALOG(R)File 155:MEDLINE(R)
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08923855 20212171 PMID: 10748683
[Lipids and AIDS]
Lipides et SIDA.
Ducobu J; Payen M C
Services de Medecine, C.H.U. Tivoli, La Louviere.
Revue medicale de Bruxelles (BELGIUM) Feb 2000, 21 (1) p11-7, ISSN 0035-3639 Journal Code: 8003474
Document type: Journal Article ; English Abstract
Languages: FRENCH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
HIV infection induces an early decrease of cholesterol and a late increase of triglycerides (TG) with a reduction of HDL. These changes are proportional with the lowering of CD4, which reflects the infection's severity. Both the increase of TG synthesis and the decrease of TG catabolism, in relation with a reduction of lipoprotein lipase activity, are responsible of these changes. Moreover, LDL catabolism is enhanced by macrophage scavenger receptors, due to a high proportion of small, dense LDL which are more easily oxidized. Many cytokines (interferon alpha, interleukins, TNF) play probably a pathogenic role in the dyslipidemia. Some HIV patients who received antiproteases may develop lipodystrophy with central obesity, insulino-resistance, glucose intolerance and sometimes diabetes (like in syndrome X). Other patients present a cushingoid, buffalo hump. This complication may be observed also with antiretroviral treatment other than antiproteases. The physiopathology of these findings could be in relation with structural homologies between antiproteases and some important proteins, involved in lipid and adipocyte metabolism. Cardiovascular risk linked to these perturbations is evident. The treatment is not different from the treatment for seronegative, hyperlipidemic patients: struggle against risk factors, diet advices, fibrates or statins. The antiproteases bring huge contribution to the prognosis of AIDS patients but the risk of cardiovascular complications could impair this therapeutic progress. So, it is essential to understand the pathogeny of these complications in order to discover new antiproteases, without these adverse side effects.
Tags: Human
Descriptors: *Acquired Immunodeficiency Syndrome--blood--BL; *Lipids --blood--BL; Acquired Immunodeficiency Syndrome--drug therapy--DT; Adipocytes--drug effects--DE; Adipocytes--metabolism--ME; CD4 Lymphocyte Count; Cholesterol--blood--BL; Cytokines--blood--BL; Diabetes Mellitus --chemically induced--CI; Glucose Intolerance--chemically induced--CI; HIV Infections--blood--BL; HIV Infections--drug therapy--DT; HIV Protease Inhibitors -- adverse effects --AE; HIV Protease Inhibitors --therapeutic use--TU; Heart Diseases--etiology--ET; Hypertriglyceridemia --blood--BL; Hypolipoproteinemia--blood--BL; Insulin Resistance ; Lipodystrophy--chemically induced--CI; Lipoproteins, HDL Cholesterol--blood --BL; Obesity--chemically induced--CI; Prognosis; Risk Factors
CAS Registry No.: 0 (Cytokines); 0 (HIV Protease Inhibitors); 0 (Lipids); 0 (Lipoproteins, HDL Cholesterol); 57-88-5 (Cholesterol)
Record Date Created: 20000425
Record Date Completed: 20000425

27/9/28
DIALOG(R)File 155:MEDLINE(R)
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08923825 20212141 PMID: 10748653

[Dysmetabolic syndrome related to HIV-1 protease inhibitors. Review of the literature and personal data]

Sindrome dismetabolica da inibitori della HIV-1 proteasi. Revisione della letteratura e dati personali.

Urso R; Croce G F; Tubili C; De Marco M; La Scala P; Luglio D; Narciso P

IV Divisione Malattie Infettive, IRCCS Lazzaro Spallanzani, Roma. ursor@tin.it

Recenti progressi in medicina (ITALY) Feb 2000, 91 (2) p78-85, ISSN 0034-1193 Journal Code: 0401271

Document type: Journal Article; Review; Review, Tutorial ; English Abstract

Languages: ITALIAN

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS; AIDS/HIV

HIV-positive patients receiving antiretroviral therapy with HIV-1 protease-inhibitors (PI) frequently show insulin-resistance, impaired glucose tolerance, hypertriglyceridaemia and lipodystrophy (LD). LD has often been reported only after the beginning of PI therapy. Some authors link LD to HIV chronic infection, some others suggest that PIs increase pre-existent disturb. Preliminary data of an observational study drawn in IV day-hospital of Spallanzani Institute in Rome showed hypertriglyceridaemia in 36.4% and hyperglycaemia in 11.2% of patients treated with PI. Carr suggests that such drugs should have this lipid-increasing effect because of their inhibition of low density lipoprotein-receptor-related protein, cytoplasmic retinoic-acid binding protein type 1 and P450 3A cytochrome. This theory doesn't explain why both untreated patients and treated with only reverse transcriptase inhibitors show sometimes the same disorders. According to another hypothesis Tumor necrosis factor-alpha, through inhibition of lipoprotein-lipase, would determine high fat-storage in the adipose tissue. Cardiovascular risk factors have always to be assessed before starting a therapy with PI. Glycaemia, triglyceridaemia, cholesterolaemia have to be performed every three months during the treatment and, if necessary, C-Peptide and insulinaemia too. A treatment with lipid-lowering drugs is always recommended in patients with hypertriglyceridaemia > 500 mg/dl and/or hypercholesterolaemia LDL > 190 mg/dl in two following checks. Fibrates have proven to be effective in reducing hypertriglyceridaemia, but there is no certainty that such therapies could have good effects on the LD itself too. (58 Refs.)

Tags: Comparative Study; Female; Human; Male

Descriptors: Diabetes Mellitus, Non-Insulin-Dependent--chemically induced --CI; * HIV Protease Inhibitors -- adverse effects --AE; *HIV-1 --enzymology--EN; *Hypertriglyceridemia--chemically induced--CI; * Insulin Resistance ; *Lipodystrophy--chemically induced--CI; Antilipemic Agents --therapeutic use--TU; Diabetes Mellitus--complications--CO; HIV Infections --drug therapy--DT; Hypertriglyceridemia--drug therapy--DT; Iatrogenic Disease; Risk Factors

CAS Registry No.: 0 (Antilipemic Agents); 0 (HIV Protease Inhibitors)

Record Date Created: 20000414

Record Date Completed: 20000414

27/9/29
DIALOG(R)File 155:MEDLINE(R)
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08814838 20097826 PMID: 10634360
Fasting hyperinsulinemia in human immunodeficiency virus-infected men: relationship to body composition, gonadal function, and protease inhibitor use.
Hadigan C; Corcoran C; Stanley T; Piecuch S; Klibanski A; Grinspoon S
Neuroendocrine Unit, Massachusetts General Hospital and Harvard Medical School, Boston, 02114, USA.
Journal of clinical endocrinology and metabolism (UNITED STATES) Jan 2000, 85 (1) p35-41, ISSN 0021-972X Journal Code: 0375362
Contract/Grant No.: F32-DK-09218; DK; NIDDK; MO1-RR-01066; RR; NCRR; R01-DK-49302; DK; NIDDK
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS; AIDS/HIV
Fat redistribution in the setting of protease inhibitor use is increasingly common and is associated with insulin resistance in human immunodeficiency virus (HIV)-infected patients. However, little is known regarding the factors that may contribute to abnormal insulin regulation in this population. We assessed fasting insulin levels in HIV-infected men and determined the relationship among insulin, body composition, endogenous gonadal steroid concentrations, and antiviral therapy in this population. We also determined the effects of exogenous testosterone administration using the homeostatic model for insulin resistance (HOMA IR) in hypogonadal HIV-infected men with the acquired immunodeficiency syndrome wasting syndrome. Fifty HIV-infected men with acquired immunodeficiency syndrome wasting were compared with 20 age- and body mass index (BMI)-matched healthy control subjects. Insulin concentrations were significantly increased in HIV-infected patients compared to those in control patients (16.6+/-1.8 vs. 10.4+/-0.8 microU/mL; P<0.05) and were increased in nucleoside reverse transcriptase (NRTI)-treated patients who did not receive a protease inhibitor (PI; 21.7+/-4.3 vs. 10.4+/-0.8 microU/mL; P<0.05). Insulin concentrations and HOMA IR were inversely correlated with the serum free testosterone concentration (r = -0.36; P = 0.01 for insulin level; r = -0.30; P = 0.03 for HOMA), but not to body composition parameters, age, or BMI. In a multivariate regression analysis, free testosterone (P = 0.05), BMI (P<0.01), and lean body mass (P = 0.04) were significant. Lower lean body mass and higher BMI predicted increased insulin resistance. The HIV-infected patients demonstrated an increased trunk fat to total fat ratio (0.49+/-0.02 vs. 0.45+/-0.02; P<0.05) and an increased trunk fat to extremity fat ratio (1.27+/-0.09 vs. 0.95+/-0.06, P = 0.01), but a reduced extremity fat to total fat ratio (0.44+/-0.01 vs. 0.49 + 0.01; P = 0.02) and reduced overall total body fat (13.8+/-0.7 vs. 17.2+/-0.9 kg; P<0.01) compared to the control subjects. Increased truncal fat and reduced extremity fat were seen among NRTI-treated patients, but this pattern was most severe among patients receiving combined NRTI and PI therapy [trunk fat to extremity ratio, 1.47+/-0.15 vs. 0.95+/-0.06 (P<0.01); extremity fat to total fat ratio, 0.40+/-0.02 vs. 0.49+/-0.01 (P<0.05)]. Insulin responses to testosterone administration were investigated among 52 HIV-infected men with hypogonadism and wasting (weight <90% ideal body weight and/or weight loss >10%) randomized to either testosterone (300 mg, im, every 3 weeks) or placebo for 6 months. Testosterone administration reduced HOMA IR in the HIV-infected men (-0.6+/-0.7 vs. +1.41+/-0.8, testosterone vs. placebo, P = 0.05) in association with increased lean body mass (P = 0.02). These data demonstrate significant hyperinsulinemia in HIV-infected patients, which can occur in the absence of PI use. In NRTI-treated patients not receiving PI, a precursor phenotype is apparent, with increased truncal fat, reduced extremity fat, and increased insulin concentrations. This phenotype is exaggerated in patients receiving PI therapy, with further increased truncal fat and reduced extremity fat, although hyperinsulinemia per se is not worse. Endogenous gonadal steroid levels are inversely related to

hyperinsulinemia in HIV-infected men, but reduced lean body mass and increased weight are the primary independent predictors of hyperinsulinemia. Indexes of insulin sensitivity improve in response to physiological androgen administration among hypogonadal HIV-infected patients, and this change is again related primarily to increased lean body mass in response to testosterone administration.

Tags: Human; Male; Support, U.S. Gov't, P.H.S.

Descriptors: Body Composition--physiology--PH; *HIV Infections--blood--BL ; * HIV Protease Inhibitors -- adverse effects --AE; *Hyperinsulinism --blood--BL; *Testosterone--blood--BL; Adipose Tissue--physiology--PH; Adult; Analysis of Variance; Blood Glucose--metabolism--ME; Body Composition--drug effects--DE; CD4 Lymphocyte Count; Cross-Sectional Studies; HIV Infections--drug therapy--DT; HIV Protease Inhibitors --therapeutic use--TU; Insulin Resistance ; Longitudinal Studies; Phenotype

CAS Registry No.: 0 (Blood Glucose); 0 (HIV Protease Inhibitors); 57-85-2 (Testosterone)

Record Date Created: 20000203

Record Date Completed: 20000203

27/9/30
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08799706 20082178 PMID: 10615316
HIV protease inhibitors, the lipodystrophy syndrome and polycystic ovary syndrome--is there a link?
Wilson J D; Dunham R J; Balen A H
Department of Genitourinary Medicine, General Infirmary at Leeds.
Sexually transmitted infections (ENGLAND) Aug 1999, 75 (4) p268-9, ISSN 1368-4973 Journal Code: 9805554
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
Tags: Case Report; Female; Human
Descriptors: HIV Protease Inhibitors -- adverse effects --AE; *Lipodystrophy--chemically induced--CI; *Polycystic Ovary Syndrome --chemically induced--CI; Adult; Genetic Predisposition to Disease; HIV Infections--complications--CO; HIV Infections--drug therapy--DT; HIV Protease Inhibitors--therapeutic use--TU; Insulin Resistance ; Lipodystrophy--genetics--GE; Polycystic Ovary Syndrome--genetics--GE
CAS Registry No.: 0 (HIV Protease Inhibitors)
Record Date Created: 20000105
Record Date Completed: 20000105

27/9/31
DIALOG(R)File 155:MEDLINE(R)
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08795942 20078350 PMID: 10612226
[Effects of high grade antiretroviral therapy on body fat distribution and metabolism]
Auswirkungen der hochaktiven antiretroviralen Therapie auf Korperschema und Stoffwechsel.
Schwenk A
Department of Infectious Disease St. George's Hospital. a.schwenk@sghms.ac.uk
Zentralblatt fur Gynakologie (GERMANY) 1999, 121 (11) p552-3, ISSN 0044-4197 Journal Code: 21820100R
Document type: Journal Article; Review; Review, Tutorial
Languages: GERMAN
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
(5 Refs.)
Tags: Female; Human; Male
Descriptors: HIV Infections--drug therapy--DT; * HIV Protease Inhibitors -- adverse effects --AE; *HIV Protease Inhibitors --metabolism--ME; *Hyperlipidemia--chemically induced--CI; * Insulin Resistance ; *Lipodystrophy--chemically induced--CI; Cardiovascular Diseases--etiology--ET; HIV Protease Inhibitors--therapeutic use--TU; Hyperlipidemia--metabolism--ME; Lipodystrophy--metabolism--ME; Syndrome
CAS Registry No.: 0 (HIV Protease Inhibitors)
Record Date Created: 20000210
Record Date Completed: 20000210

27/9/32
DIALOG(R)File 155:MEDLINE(R)
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08778604 20060445 PMID: 10592860
Adverse metabolic disorders during highly active antiretroviral treatments (HAART) of HIV disease.
Vigouroux C; Gharakhanian S; Salhi Y; Nguyen T H; Adda N; Rozenbaum W; Capeau J
Service de Biochimie, Hopital Rothschild, Paris, France. capeau@st-antoine.inserm.fr
Diabetes & metabolism (FRANCE) Nov 1999, 25 (5) p383-92, ISSN 1262-3636 Journal Code: 9607599
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
Protease inhibitor treatment has dramatically improved rates of morbidity and mortality in HIV-infected patients. However, it has recently been shown that this medication is associated with long-term side effects characterized by metabolic, clinical and biological alterations. These modifications have been described in patients treated with highly active antiretroviral therapy (HAART), including nucleoside analogue reverse transcriptase inhibitors (NRTI) and generally (but not always) protease inhibitors (PI). Clinical alterations are characterised by a body fat redistribution syndrome or lipodystrophy, with peripheral lipoatrophy and/or central fat accumulation. They are often associated with biological alterations, i.e. insulin resistance, hyperglycaemia and dyslipidaemia, which can also be observed alone. The pathophysiology of these alterations is presently unknown. The deleterious effect of PI on adipose tissue could be direct or indirect, and is probably modulated by genetic or environmental factors. NRTI could also be involved because of their mitochondrial toxicity. The purpose of the treatment is to control metabolic disturbances in order to prevent immediate complications such as acute pancreatitis and limit possible cardiovascular and diabetic complications at longer term. Studies are in progress to evaluate the possibility of therapeutic alternatives to PI when major metabolic disturbances are present. (97 Refs.)
Tags: Human
Descriptors: *Anti-HIV Agents--adverse effects--AE; *HIV Infections--drug therapy--DT; *Metabolic Diseases--chemically induced--CI; HIV Protease Inhibitors -- adverse effects --AE; Hyperglycemia--chemically induced --CI; Hyperlipidemia--chemically induced--CI; Insulin Resistance ; Metabolic Diseases--physiopathology--PP; Metabolic Diseases--therapy--TH; Reverse Transcriptase Inhibitors--adverse effects--AE
CAS Registry No.: 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors); 0 (Reverse Transcriptase Inhibitors)
Record Date Created: 19991228
Record Date Completed: 19991228

27/9/33
DIALOG(R)File 155:MEDLINE(R)
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08764342 20045571 PMID: 10578609
[The chronicity of HIV infection]
Chronicite de l'infection par le VIH.
Morlat P
Service de medecine interne et maladies infectieuses Hopital Saint-Andre, Bordeaux.
La Revue du praticien (FRANCE) Oct 15 1999, 49 (16) p1781-5, ISSN 0035-2640 Journal Code: 0404334
Document type: Journal Article ; English Abstract
Languages: FRENCH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
The widespread use of highly active antiretroviral therapy led to a substantial decrease of HIV related-morbidity and mortality in industrialized countries. These recent advances allow to envisage a chronicity of HIV infection and led HIV infected people to set up a familial or professional life-project, difficult to imagine until now. The increase in life-expectancy is nevertheless closely dependent on the prolonged adherence of the patients to therapy, which justifies the development of strategies to increase medication compliance. The side-effects of long-term taken drugs often impair the quality of life of HIV infected people: abnormal fat distribution and atherogen hyperlipidemia and insulin resistance, mainly described with protease inhibitors, are new worrying concerns. Chronicity of HIV infection favours also the development of co-morbidity (HIV-HCV co-infection). The necessity of a more global and varied case management of people living with HIV is emerging simultaneously with a new dynamic of clinical research whose ultimal goal still remains the achievement of HIV eradication strategies.
Tags: Human
Descriptors: *HIV Infections--physiopathology--PP; AIDS-Related Opportunistic Infections--physiopathology--PP; Adipose Tissue--drug effects --DE; Anti-HIV Agents--adverse effects--AE; Anti-HIV Agents--therapeutic use--TU; Case Management; Chronic Disease; Connective Tissue Diseases --chemically induced--CI; Developed Countries; HIV Infections--drug therapy --DT; HIV Infections--prevention and control--PC; HIV Infections --psychology--PX; HIV Protease Inhibitors -- adverse effects --AE; Hyperlipidemia--chemically induced--CI; Insulin Resistance ; Life Expectancy; Patient Compliance; Quality of Life; Survival Rate
CAS Registry No.: 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors)
Record Date Created: 19991222
Record Date Completed: 19991222

29/9/1
DIALOG(R)File 155:MEDLINE(R)
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14624966 22517127 PMID: 12630645

Lipodystrophy, insulin resistance , diabetes mellitus, dyslipidemia, and cardiovascular disease in human immunodeficiency virus infection.

Tanwani Lal K; Mokshagundam SriPrakash L

University of Louisville and Veterans Affairs Medical Center, Louisville, KY, USA. manoharlal626@pol.net

Southern medical journal (United States) Feb 2003, 96 (2) p180-8; quiz 189, ISSN 0038-4348 Journal Code: 0404522

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

The introduction of highly active antiretroviral therapy has significantly reduced morbidity and mortality in patients infected with the human immunodeficiency virus. Treatment with antiretroviral agents--protease inhibitors in particular--has uncovered a syndrome of abnormal fat redistribution, dyslipidemia, and impaired glucose metabolism, collectively termed lipodystrophy syndrome. The cause of the syndrome seems to be multifactorial; however, its exact mechanisms have yet to be elucidated. Accelerated risk for cardiovascular disease is likely to be a major concern in these patients in the future. At this time, no clinical guidelines are available for the prevention and/or the treatment of lipodystrophy syndrome. The available treatment options range from switching the different antiretroviral drugs and lifestyle modifications to the use of pharmacologic agents to treat patients with dyslipidemia, impaired glucose tolerance and/or diabetes, and changes in body composition. This review emphasizes the clinical features, potential molecular mechanisms, and treatment options for patients infected with human immunodeficiency virus who have lipodystrophy syndrome. (66 Refs.)

Tags: Human

Descriptors: Anti - HIV Agents -- adverse effects --AE; *Anti-HIV Agents--therapeutic use--TU; *Cardiovascular Diseases--etiology--ET; *Cardiovascular Diseases--physiopathology--PP; *HIV Infections --complications--CO; *HIV Infections--drug therapy--DT; *HIV-Associated Lipodystrophy Syndrome--etiology--ET; *HIV-Associated Lipodystrophy Syndrome--physiopathology--PP; *Hyperlipidemia--etiology--ET; *Hyperlipide mia--physiopathology--PP; *Insulin Resistance--physiology--PH; Cardiovascul ar Diseases--therapy--TH; HIV Infections--physiopathology--PP; HIV-Associated Lipodystrophy Syndrome--therapy--TH; Hyperlipidemia--therapy --TH

CAS Registry No.: 0 (Anti-HIV Agents)

Record Date Created: 20030312

Record Date Completed: 20030325

29/9/2
DIALOG(R)File 155:MEDLINE(R)
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11983882 99428979 PMID: 10499191
Diabetes, insulin resistance and dyslipidaemia in lipodystrophic HIV-infected patients on highly active antiretroviral therapy (HAART).
Vigouroux C; Gharakhanian S; Salhi Y; Nguyen T H; Chevenne D; Capeau J; Rozenbaum W
Service de Biochimie, Hopital Rothschild, Paris, France.
Diabetes & metabolism (FRANCE) Sep 1999, 25 (3) p225-32, ISSN 1262-3636 Journal Code: 9607599
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
This study assessed glucose tolerance, insulin sensitivity and lipid parameters in HIV-infected patients presenting with lipodystrophy during HAART including protease inhibitors. Fourteen consecutive patients from Rothschild Hospital treated with HAART and presenting with marked facial lipoatrophy were evaluated. A 75 g oral glucose tolerance test (OGTT) with measurement of plasma glucose, insulin, proinsulin and free fatty acids at T0, 30, 60, 90 and 120 min was performed. Lipid parameters (triglycerides, cholesterol, apolipoproteins A1 and B) were studied as well as nutritional and inflammatory markers (albumin, prealbumin, transferrin, haptoglobin, orosomucoid, C-reactive protein), endocrine and cytokine parameters (thyrotropin, cortisol, leptin, interleukin-6), HIV viral load and CD4-lymphocyte count. These patients were compared with 20 non-lipodystrophic protease inhibitor-treated patients. The measurements performed during OGTT showed that among the 14 lipodystrophic patients, 11 (79%) presented with diabetes (5 patients) or normal glucose tolerance but with insulin resistance (6 patients). This frequency was strikingly different in the group of nonlipodystrophic patients, which included only 4 (20%) presenting with diabetes (1 patient), or impaired glucose tolerance (2 patients), or normal glucose tolerance but with insulin resistance (1 patient). Hypertriglyceridaemia was present in 11 lipodystrophic (79%) versus 7 nonlipodystrophic patients (35%). Nutritional and endocrine measurements were normal. An abnormal processing of proinsulin to insulin was excluded. Thus, lipodystrophy during HAART was associated with diabetes, insulin resistance and hypertriglyceridaemia. Diabetes, diagnosed by basal and/or 120 min-OGTT glycaemia, seems more frequent than previously described. The therapeutic consequences of these results deserve evaluation in clinical trials.
Tags: Female; Human; Male
Descriptors: Anti - HIV Agents -- adverse effects --AE; *Diabetes Mellitus--etiology--ET; *HIV Infections--drug therapy--DT; *HIV Protease Inhibitors--adverse effects--AE; *Hyperlipidemia--etiology--ET; *Insulin Resistance; *Lipodystrophy--chemically induced--CI; Adult; Aged; Apolipoproteins--blood--BL; Blood Glucose--metabolism--ME; Cholesterol --blood--BL; Drug Therapy, Combination; Fatty Acids, Nonesterified--blood --BL; Glucose Tolerance Test; Insulin--blood--BL; Lipodystrophy --physiopathology--PP; Middle Age; Proinsulin--blood--BL; Retrospective Studies; Triglycerides--blood--BL
CAS Registry No.: 0 (Anti-HIV Agents); 0 (Apolipoproteins); 0 (Blood Glucose); 0 (Fatty Acids, Nonesterified); 0 (HIV Protease Inhibitors); 0 (Triglycerides); 11061-68-0 (Insulin); 57-88-5 (Cholesterol); 9035-68-1 (Proinsulin)
Record Date Created: 19991018
Record Date Completed: 19991018

29/9/3
DIALOG(R)File 155:MEDLINE(R)
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11856495 99297598 PMID: 10371188
Effects of metformin on insulin resistance and central adiposity in patients receiving effective protease inhibitor therapy.
Saint-Marc T; Touraine J L
AIDS (London, England) (ENGLAND) May 28 1999, 13 (8) p1000-2, ISSN 0269-9370 Journal Code: 8710219
Document type: Clinical Trial; Letter; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
Tags: Female; Human; Male
Descriptors: *Adipose Tissue--drug effects--DE; *HIV Protease Inhibitors --adverse effects--AE; *Hypoglycemic Agents--therapeutic use--TU; *Insulin Resistance; *Metformin--therapeutic use--TU; Adult; Anti - HIV Agents -- adverse effects --AE; Anti-HIV Agents--therapeutic use--TU; Body Composition; HIV Infections--drug therapy--DT; HIV Protease Inhibitors --therapeutic use--TU; Insulin--blood--BL
CAS Registry No.: 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors); 0 (Hypoglycemic Agents); 11061-68-0 (Insulin); 657-24-9 (Metformin)
Record Date Created: 19990902
Record Date Completed: 19990902

29/9/4
DIALOG(R)File 155:MEDLINE(R)
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09738648 21540246 PMID: 11684939
Where does insulin resistance in lipodystrophic HIV-1-positive subjects come from?
Schmidt H H
AIDS (London, England) (England) Nov 9 2001, 15 (16) p2187-8, ISSN 0269-9370 Journal Code: 8710219
Comment on AIDS. 2001 Nov 9;15(16) 2093-100; Comment on PMID 11684928
Document type: Comment; Editorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
Tags: Human
Descriptors: Anti - HIV Agents -- adverse effects --AE; *HIV Infections--complications--CO; *Insulin Resistance; *Lipodystrophy --chemically induced--CI; *Protease Inhibitors--adverse effects--AE; Glucose--metabolism--ME; HIV Infections--drug therapy--DT; HIV-1
CAS Registry No.: 0 (Anti-HIV Agents); 0 (Protease Inhibitors); 50-99-7 (Glucose)
Record Date Created: 20011030
Record Date Completed: 20020118

29/9/5
DIALOG(R)File 155:MEDLINE(R)
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09693413 21485801 PMID: 11600834
Getting to the HAART of insulin resistance .
Nolan D; Mallal S
AIDS (London, England) (England) Oct 19 2001, 15 (15) p2037-41,
ISSN 0269-9370 Journal Code: 8710219
Comment on AIDS. 2001 Oct 19;15(15) 1993-2000; Comment on PMID 11600828
Document type: Comment; Editorial; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV
(39 Refs.)
Tags: Human
Descriptors: Anti - HIV Agents -- adverse effects --AE; *Antiretroviral Therapy, Highly Active--adverse effects--AE; *HIV Infections--drug therapy--DT; *HIV Protease Inhibitors--adverse effects--AE; *Insulin Resistance; *Lipodystrophy--physiopathology--PP; Lipodystrophy --etiology--ET; Reverse Transcriptase Inhibitors--adverse effects--AE
CAS Registry No.: 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors); 0 (Reverse Transcriptase Inhibitors)
Record Date Created: 20011015
Record Date Completed: 20020103